CLINICAL RESEARCH

Survival of Replanted Permanent Teeth after Traumatic Avulsion

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ABSTRACT

Introduction: Tooth replantation is the treatment of choice for avulsion, even though its long-term prognosis shows great variability and few studies have adopted survival analysis to evaluate the fate of such teeth. The present study aimed to evaluate both the survival rate of replanted permanent teeth after traumatic avulsion as well as its clinical and demographic determinants. **Methods:** Records from 576 patients treated at the Dental Trauma Clinic at the Federal University of Minas Gerais, Brazil, were analyzed to collect clinical and radiographic data. Kaplan-Meier curves and a multivariate Cox regression model were used to estimate the probability of replanted teeth remaining functional in the mouth and to determine prognostic factors. **Results:** The post-replantation survival rate was 50% after 5.5 years. Immature teeth presented an increase of 51.3% in the loss rate ($P = .002$). Each additional year in the patient's age at the time of trauma, up to the limit of 16 years, reduced the loss rate of replanted teeth by 15% ($P < .001$). The storage of the avulsed teeth in milk decreased the loss rate of replanted teeth by 56.4% ($P = .015$) when compared with those kept dry. **Conclusions:** The overall survival rate after replantation of permanent teeeth was 50% after 5.5 years. Advanced stages of root development, together with the increase in the patient's age at the moment of trauma, up to the limit of 16 years, were good prognostic factors for tooth survival. The storage of avulsed teeth in milk was also associated with enhanced tooth survival after replantation. *(J Endod 2019;■:1–6.)*

KEY WORDS

Milk; storage medium; survival analysis; tooth avulsion; tooth replantation

SIGNIFICANCE

A survival rate of 50% after 5.5 years for replanted permanent teeth was demonstrated. Stage of root development was an important prognostic factor. Original clinical evidence of milk as a favorable storage medium for avulsed tooth was also provided.

Tooth avulsion is a serious traumatic dental injury (TDI), with prevalence in permanent dentition ranging from 0.5%–16.0%[1,2]. Replantation of avulsed permanent teeth is still the desirable treatment option, especially in growing patients. However, the long-term prognosis shows great variability because it is affected by several factors related to the immediate management of the avulsed tooth as well as to the emergency and sequential treatment[2–5].

The clinical dental literature regarding the fate of avulsed/replanted teeth is still dominated by isolated case reports and cross-sectional retrospective studies that lack standardization of evaluated outcomes as well as of statistical treatment of the data. In addition, most longitudinal clinical studies have evaluated the role of clinical and demographic determinants in different periodontal healing patterns that cannot necessarily be translated into replantation success/failure rates. This fact makes comparisons of results, data pooling, and overall conclusions very difficult[6]. To overcome these shortcomings, survival analysis has been suggested as the ideal approach for replantation studies because it allows inclusion of patients with different follow-up times[7]. Few studies have adopted this methodology to evaluate the long-term prognosis of replanted teeth. Andreasen et al[8] conducted the first prospective study with 400 replanted permanent teeth that were followed for a mean period of 5.1 years. There was an overall tooth loss rate of 30%, which was significantly higher for teeth with incomplete root development (55%) when compared with mature teeth (45%)[8]. Barrett and Kenny[9] reported a frequency of tooth loss of 25% in a sample comprising 52 replanted teeth. The relative risk of failure was significantly greater for immature teeth, in patients younger than 11 years, and for those who required prolonged calcium hydroxide therapy. Pohl et al[10] reported an estimated survival of 4.7 years in a sample of 28 teeth replanted after extraoral endodontic treatment and retrograde insertion of posts. Tooth loss/extraction comprised 35% and was associated with storage condition. Differences in the survival expectation were not significant when mature and immature teeth were compared. A total of 31.3% of tooth loss/extraction was observed

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by Petrovic et al[11] in a sample comprising 32 replanted teeth, with a median survival period of 2.5 years. The stage of root development at the time of replantation was the only variable that affected tooth survival. In a study by Wang et al[12], a sample of 196 teeth was followed for a mean period of 4 years. A total of 46 teeth (23.5%) were lost/extracted by the end of the study; most of them were immature teeth. The median survival period for each group was given graphically, and as could be estimated from the pictures, the periods were 5.5 years for immature teeth and 11 years for mature teeth.

The present study aimed to conduct a survival analysis of replanted permanent teeth and determine their clinical and demographic prognostic factors, among patients treated at the Dental Trauma Clinic in the School of Dentistry, Federal University of Minas Gerais, Belo Horizonte, Brazil.

MATERIALS AND METHODS

The present sample comprised avulsed and replanted permanent teeth from patients treated in the Dental Trauma Program at the Federal University of Minas Gerais in Belo Horizonte, Brazil from 1994–2018. Emergency care was provided at the Metropolitan Hospital Odilon Behrens. Thereafter, patients were referred to the Dental Trauma Clinic in the School of Dentistry UFMG, where they underwent sequential treatment and follow-up. Both centers participate in the multidisciplinary Dental Trauma Program at UFMG and in 1994 adopted the same protocol to manage TDIs[13]. Replantation steps were the following: the avulsed tooth was kept in Hanks' balanced salt solution, and the socket was copiously irrigated with saline. The tooth was then held by the crown, avoiding any manipulation of the root surface, and gently repositioned by using light digital pressure on the buccal and palatal sides of the alveolar process. After tooth repositioning, a radiograph was taken to verify the position, and the tooth was splinted with orthodontic wire (Ø 0.8 mm) and composite resin. Root development was evaluated from periapical radiographs taken at the replantation visit and classified according to the stages described by Moorrees et al[14]. Teeth with stages 1–4, corresponding to root length development in quarters, were classified as immature. Teeth showing full root length with the apical foramen half closed were classified as stage 5. Teeth showing full root development with closed apex were classified as stage 6. Pulpectomy and splint removal were performed after a minimum period of 15 days in the Dental Trauma Clinic at UFMG.

TABLE 1 - Sample Distribution according to Pulpal Status and Stage of Root Development

	Stage of root development					
Pulpal status	**2 n (%)**	**3 n (%)**	**4 n (%)**	**5 n (%)**	**6 n (%)**	**Total N (%)**
Pulp survival	1 (10)	1 (4.3)	2 (4.9)	1 (2.7)	0	5 (0.9)
Pulp canal obliteration	1 (10)	1 (4.3)	0	1 (2.7)	0	3 (0.5)
Pulp bone	2 (20)	4 (17.4)	4 (9.8)	1 (2.7)	0	11 (1.9)
Necrosis	6 (60)	17 (73.9)	35 (85.4)	34 (91.9)	465 (100.0)	557 (96.7)
Total	10	23	41	37	465	576 (100.0)

After pulpectomy, the root canals of mature teeth received a calcium hydroxide dressing for at least 4 weeks, and then if there were no clinical or radiographic signs of infection, they were filled with gutta-percha and sealer. The patients were examined every 3 months during the first year and annually thereafter. Calcium hydroxide therapy was continued after the first month if there were signs of persistent infection (inflammatory external root resorption- [IERR], fistula, and progressive crown discoloration) or in immature teeth to promote apexification. Periapical radiograph standardization was based on established criteria found in literature described elsewhere[15]. Survival of replanted teeth was defined as the length of time a replanted tooth remained functional after replantation, that is, the tooth remained in the mouth with no signs of infection or infra-positioning with arrested alveolar bone development[16–18]. This evaluation was based on clinical and radiographic evidence found during follow-up. Periodontal healing was radiographically evaluated at the last follow-up visit, assessing the presence and type of external root resorption (ERR). Resorption was classified either as IERR or as replacement ERR [RERR], according to the criteria of Andreasen et al[8]. The extent of ERR was also assessed by using the root resorption index developed by Andersson et al[19]. Pulpal status was classified as pulp necrosis, pulp canal obliteration, pulp bone and pulp survival without radiographic changes, following criteria described by Andreasen et al[8]. Clinical and demographic variables such as patient's age at the time of trauma, stage of root development, extra-alveolar period and storage conditions of the avulsed teeth, systemic antibiotic therapy (SAT) prescription, splinting period, timing of pulpectomy, and definitive obturation of root canal were also retrospectively collected from patientś records. Exclusion criteria were concomitant root or alveolar process fractures, replanted tooth with previous events of trauma, extensive restorations, endodontically treated, or with radiographic signs of root resorption before the injury. Those patients with a second event of trauma occurring during the follow-up period had their data collected up to the event of the second trauma. This study was approved by the Committee on Ethics in Research of the UFMG (COEP-UFMG - 2.756.614).

Statistical Analysis

Kaplan-Meier curves were used to estimate survival after replantation and to determine the probability of replanted teeth remaining in the oral cavity during the follow-up period. The nonparametric log-rank test was used to compare survival curves for categorical variables (gender, SAT prescription, concomitant crown fractures, tooth group, and stage of root development). Because there were missing data for the covariates SAT prescription, extra-alveolar period, and storage condition, multiple imputation was used via the Multiple Imputation by Chained Equations (MICE) package in R, so that individuals missing that information could be included in the analysis[20]. The Cox proportional hazards model was used to explore nominal associations of continuous factors with risk of loss/extraction. The status of immobilization and endodontic therapy changed during the follow-up period, and they came to be treated as time-dependent covariates. The extra-alveolar period was logarithmically transformed because of its great asymmetry. A spline-based strategy demonstrated that the covariate patient's age at trauma had a non-linear effect. Therefore, it was split into 2 linear

TABLE 2 - Causes of Tooth Loss/Extraction

	n (%)
RERR	32 (22.7)
IERR	21 (14.9)
Infraocclusion	38 (27.0)
Cervical root fracture	27 (19.2)
Others	23 (16.2)
Total	141 (100.0)

TABLE 3 - Pulpal Status among Censored and Lost/Extracted Teeth

Pulpal healing	Lost/extracted n (%)	Censored n (%)	Total N (%)
Pulp survival	0	5 (1.2)	5 (0.9)
Pulp canal obliteration	0	3 (0.7)	3 (0.5)
Pulp bone	3 (2.1)	8 (1.8)	11 (1.9)
Necrosis	138 (97.9)	419 (96.3)	557 (96.7)
Total	141 (100)	435 (100)	576 (100)

components considering the cutoff point of 16 years, according to previous literature[15,19]. Independent variables were entered into the final multivariate Cox model on the basis of their statistical significance in the univariate analysis ($P \leq .30$). Goodness of fit based on the Schoenfeld residuals test was used to verify the proportional hazards assumption. The level of significance was set at $P < .05$. Statistical analysis was performed by using the R software (version 3.5.3; Vienna, Austria, 2018).

TABLE 4 - Cox Regression Model-Univariate and Multivariate Analysis of Potential Predictors of Tooth Survival after Replantation

Prognostic factor	Univariate analysis	Multivariate analysis
	HR (95% CI), *P*	
Gender		
Female	Reference	
Male	0.86 (0.51–1.21), *P* = .40	
Patient's age at trauma*		
<16	**0.87 (0.80–0.94), *P* .001**	**0.85 (0.79–0.92), *P* < .001***
≥16	**1.12 (1.01–1.22), *P* = .03**	0.98 (0.92–1.03), *P* < .216
Systemic antibiotic therapy		
No	Reference	
Yes	0.95 (0.40–1.50), *P* = .72	
Concomitant crown fractures		
No	Reference	
Yes	0.88 (0.78–1.63), *P* = .50	
Tooth group		
Central upper incisors	Reference	
Lateral upper incisors	0.81 (0.48–1.37), *P* = .72	
Mandibular incisors	0.58 (0.19–1.72), *P* = .32	
Extra-alveolar period		
Each additional day	**1.13 (0.97–1.30), *P* = .09**	
Stage of root development		
Incomplete	Reference	
Complete	**0.58 (0.39–0.87), *P* = .008**	**0.513 (0.34–0.38), *P* = .002†**
Storage condition		
Dry	Reference	Reference
Water	0.88 (0.36–1.40), *P* = .62	0.79 (0.46–1.35), *P* = .387
Saline	0.85 (0.35–1.35), *P* = .52	0.85 (0.52–1.40), *P* = .518
Saliva	**0.58 (0.08–1.07), *P* = .28**	0.5 (0.17–1.46), *P* = .203
Milk	**0.63 (0.18–1.06), *P* = .05**	**0.56 (0.25–0.89), *P* = .015†**
Timing of endodontic therapy steps		
None (pulpal healing)	Reference	
Time until pulpectomy	1.52 (0.36–6.43), *P* = .56	
Timing of CaOH dressing	2.11 (0.67–6.64), *P* = .20	
Timing after obturation	0.52 (0.14–1.96), *P* = .33	
Splinting		
None	Reference	
Timing with splint	0.21 (0.002–1.45), *P* = .14	
Time without splint	0.38 (0.003–6.26), *P* = .42	

*Multivariate model including 2 linear components for the continuous covariate patient's age at trauma, extra-alveolar period and storage condition.
†Multivariate model including stage of root development, extra-alveolar period and storage condition.
Covariates that entered the multivariate model and remained significant in the final multivariate model are indicated in bold.

RESULTS

Records of 871 patients with 1288 replanted permanent teeth were analyzed. After applying the exclusion criteria, the final sample comprised 576 patients, 394 males (68.4%) and 182 females (31.6%), with a mean age of 13.3 ± 6.9 years (range, 5.1–73.2 years) at the moment of trauma. A total of 767 permanent replanted teeth after avulsion were followed up for a median period of 2.7 years. Considering that 145 patients suffered avulsion in more than 1 tooth and that time to event/censoring was strongly correlated among teeth from the same patient, only 1 tooth was randomly selected to better set convergence criteria in the statistical models. Therefore, the final sample consisted of 576 teeth. Five hundred two teeth (87.0%) had complete root formation (stages 5 and 6), and 74 teeth (13.0%) were classified as immature teeth (stages 2, 3, and 4). The extra-alveolar period ranged from 5 minutes–7 days (median period, 120 minutes), and only 40 teeth (7.1%) were replanted within 15 minutes of the trauma event. Sample distribution regarding the storage condition showed that 233 teeth (41.2%) were stored dry, 133 (23.5%) were stored in milk and 105 (18.6%) in saline solution. Water (13.4%) and saliva (3.3%) were also used as storage media. SAT was prescribed in 17.4% of the cases. The medium time elapsed from replantation to pulp extirpation was 60 days, and the medium period of CaOH intracanal dressing was 1 year. The median splinting duration was 48 days (range, 15 days–5 years). Necrosis was the most frequent pulpal outcome and was observed in 96.7% of the cases. Pulp canal obliteration was observed in 3 teeth (0.5%), bone ingrowth into the root canal was observed in 11 teeth (1.9%), and pulp survival without radiographic changes was observed in 5 teeth (0.9%). Pulpal healing was only observed in immature teeth, because it was inversely proportional to root development (Table 1). Periodontal healing was observed in only 8.9% of the sample (51 teeth), whereas ERR was observed in almost all cases (525 teeth, 91.1%), most of them with RERR (379 teeth, 65.8%). IERR was observed in 145 cases (25.4%).

Survival Analysis

By the end of the present study, 435 of the 576 replanted teeth (85.5%) being followed up were censored, and 141 (24.5%) were lost/extracted because of different causes presented in Table 2. Tooth loss/extraction

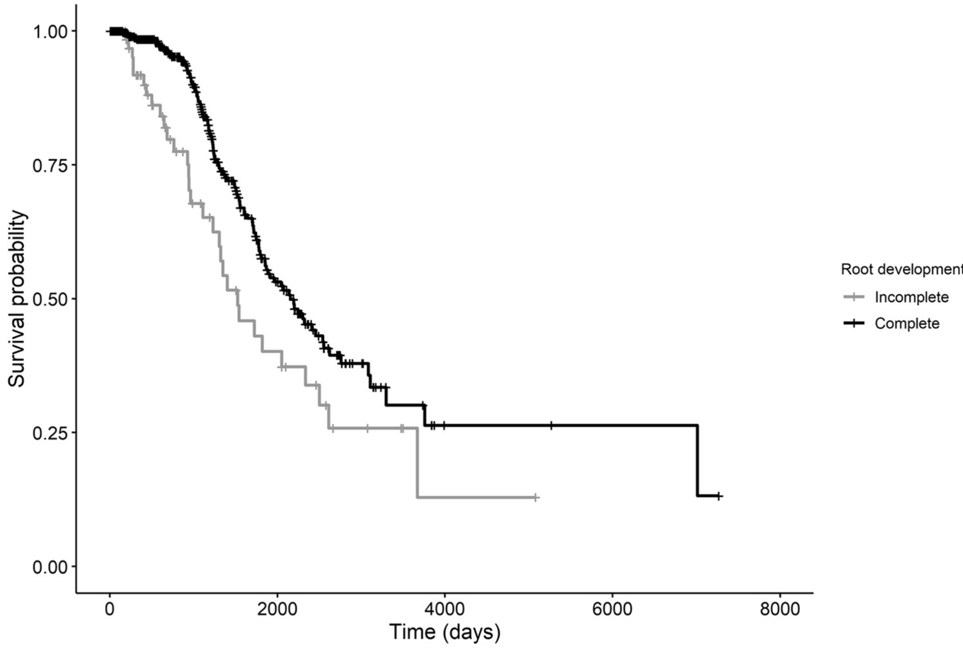

FIGURE 1 – Kaplan-Meier survival curves for root development. Replanted permanent teeth with incomplete root development had lower survival rate compared with those with complete root development ($P = .002$).

was a rare event among teeth with pulpal healing (Table 3), and a global median survival of 5.5 years was observed.

Table 4 shows univariate and multivariate analyses of potential predictors of tooth survival after replantation. The univariate analysis showed that gender, prescription of SAT, tooth group, concomitant crown fractures in the avulsed tooth, length of extra-alveolar period, timing of pulpectomy, obturation, and splinting were not significant predictors of replanted tooth survival. Patient's age at trauma and stage of root development were nominally significant predictors ($P \leq .05$). Considering that patient's age and the stage of root development are closely correlated, these 2 variables were tested separately in distinct multiple Cox regression models including extra-alveolar storage condition because its nominal P value was $< .30$. In the first model, the increase of 1 year of age reduced the rate of replanted tooth loss/extraction for patients younger than 16 (hazard ratio [HR] = 0.894; 95% confidence interval [CI], 0.79–0.92;

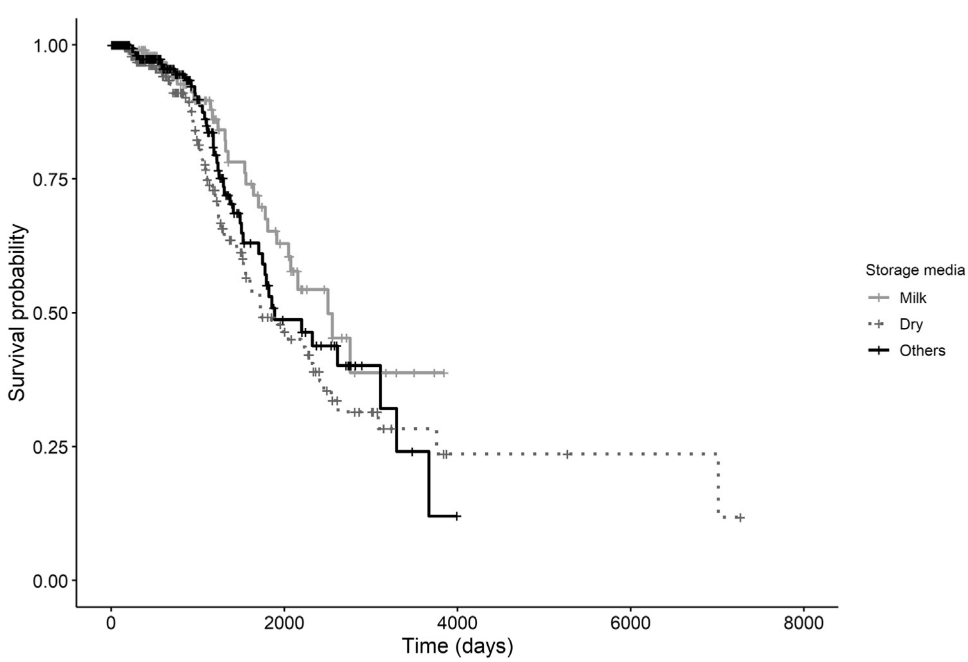

FIGURE 2 – Kaplan-Meier survival curves for storage condition. Survival expectation for teeth stored in milk was significantly higher when compared with those kept dry during the extra-alveolar period ($P = .015$).

$P < .001$). Beyond this limit, patient's age at the moment of trauma did not affect the survival of replanted permanent teeth ($P = .216$). In the second model including the stage of root development, the loss/extraction rate for replanted teeth with full length of root development was half of that for immature teeth (HR = 0.513; 95% CI, 0.34–0.38; $P = .002$). The survival rate for immature teeth was 50% after 4.2 years, and the survival rate for mature teeth was 50% after 5.5 years. In both models, the survival expectation for teeth stored in milk was significantly higher when compared with those kept dry during the extra-alveolar period (HR = 0.564; 95% CI, 0.35–0.89; $P = .015$). Storage in other media did not affect long-term maintenance of replanted teeth. Kaplan-Meier curves comparing survival function, considering the categorical variables stage of root development and storage condition, are shown in Figures 1 and 2, respectively.

DISCUSSION

The present study retrospectively evaluated the survival of permanent teeth that were replanted after traumatic avulsion. Few studies have conducted survival analysis, despite the importance of quantitative information about replantation prognosis to support treatment decision-making. Survival analysis presents an interesting approach because it consists of the evaluation of the time interval until a given event of interest. In addition, survival analysis is convenient for longitudinal evaluation of traumatized teeth, because it allows the incorporation of censored data, with partial observation of the response, into the statistical analysis. This is particularly useful because of the long periods required to reach a reasonable sample size for clinical research in dental trauma[21,22]. It is worth noting the unique features of our sample regarding its huge size and control of confounding factors related to replantation procedures during emergency care.

The tooth loss/extraction rate of 24.5% observed by the end of the present study is consistent with previous survival analyses showing tooth loss rates ranging from 23% to 35.7%[8–12]. The overall survival expectation observed in the present sample was 50% after 5.5 years, which is closer to the 4.7 years reported by Pohl et al[10]. However, it is different from the 2.5 years reported by Petrovic et al[11] and the 5.5 years for immature teeth and 11 years for teeth with full length of root development reported by Wang et al[12].

The results of the present study also demonstrated that the increase in patient's age at the moment of trauma, up to16 years, was associated with a better prognosis. In addition, the survival rate for replanted mature teeth was significantly higher as well as for those stored in milk. These findings are consistent with previous reports showing that replanted mature teeth have higher survival expectancy[8,9,11,12]. Although evaluated outcomes were different, the present results are also consistent with those from a single previous longitudinal study showing that dry storage, in contrast to milk, as well as immature roots and younger patients' age at trauma, increased the risk of tooth loss after replantation[23]. The present results showing the increased survival rate of teeth stored in milk are also consistent with a vast experimental literature demonstrating that milk is a suitable storage medium for avulsed teeth because of its unique combination of nutrients and physiological pH of 6.5–7.2[24–26].

Results of the present study suggest that SAT did not affect the long-term survival of avulsed teeth. Although some experimental results have suggested that SAT prescription may reduce IERR in replanted permanent teeth[27,28], to date, clinical evidence regarding the benefits of SAT in the periodontal healing or in the long-term fate of replanted teeth is inconclusive[8,10–12,15,29,30]. However, this area demands further investigation because clinical studies, including the present one, diverge or lack important details such as the type, dosage, and duration of antibiotics prescribed. In addition, no studies have assessed patient compliance with the treatment.

An unexpected finding of the present study was the fact that neither the extra-alveolar period nor the timing of endodontic therapy steps (pulpectomy, CaOH dressing, and definitive filling) affected the survival rate after replantation. Taken together, these findings bring up a recurrent question regarding the evaluation of replantation outcomes. Although there is no doubt that the above-mentioned factors do affect the periodontal healing patterns after replantation, the corollary that these associations are reflected in the survival of replanted teeth was not confirmed by the current results. In the present study, survival function was an objective measure defined as the interval that a replanted tooth remained functional without any signs of infection or local arrest of alveolar bone growth. Such criteria are supported by the concept that keeping a replanted tooth, even if periodontal healing patterns have not been ideal, can be considered successful replantation provided it does not compromise bone maintenance for future definitive rehabilitation in growing patients[16–18]. Although RERR represented a common finding in the present sample, RERR did not necessarily imply tooth loss/extraction. Although there is a risk of late sequelae such as infraocclusion and impairment of local bone growth, RERR cannot be considered a pathologic process *per se* and may allow maintaining the tooth for longer periods before removal becomes necessary. ERR is diagnosed during the follow-up after replantation. For this reason, it could not be treated statistically as a prognostic factor in the survival analysis because, by definition, such factors must be measured in the baseline, ie, at the time of replantation. Future investigations exploring other longitudinal models to evaluate long-term prognosis of distinct periodontal healing patterns of replanted teeth are needed and may provide relevant information to support treatment decisions.

CONCLUSION

Results of the present study showed that the overall survival rate of avulsed/replanted permanent teeth was 50% after 5.5 years. Increase in patient's age at the moment of trauma and the stage of root development were important prognostic factors for tooth survival after replantation. In addition, storage of avulsed teeth in milk during the extra-alveolar period enhanced the survival expectancy after replantation.

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