

Original article

Cancer survivors present significantly lower long-term stability of orthodontic treatment: a prospective case–control study

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Summary

Background/Objectives: The aim of the study was to compare the stability of orthodontic treatment in cancer survivors who had been treated with cytotoxic drugs with a generally healthy control group.

Materials/Methods: The study included 52 cancer survivors treated orthodontically and 52 healthy control subjects matched for age, gender, and malocclusion. The weighted Peer Assessment Rating (w-PAR) index, the Index of Complexity, Outcome and Need (ICON) were assessed before treatment, after the treatment, and at the 3-year follow-up. Patients Satisfaction Score was assessed after the treatment and at the 3-year follow-up. A repeated analysis of variance test was used to check the statistical significance between the scores.

Results: Ideal occlusion was achieved in all patients. The mean w-PAR and ICON values were significantly reduced in both groups after the end of the orthodontic treatment with no significant differences between the groups regarding the obtained results. However, after the 3-year follow-up, only the cancer survivors' group presented statistically significant ($P < 0.001$) increase of the w-PAR and ICON values comparing to the values obtained at the end of the treatment. There was no significant change in Patients' Satisfaction Score within 3 years after treatment.

Limitations: The limited size of the study sample as well as different types of oncological diagnoses could have had an impact on the final results of the study.

Conclusions/Implications: Previous cytotoxic drug treatment significantly decreases the stability of orthodontic treatment among the cancer survivors, particularly within first 12 months after the end of the treatment.

Introduction

The number of children diagnosed with cancer is increasing worldwide each year (1–4). Due to the fact that many low-income and middle-income countries do not collect the relevant data, the exact incidence of children cancer is unknown (1). It is estimated that the incidence rates of cancer among European children range from 140

to 170 per million person-years (for children younger than 15 years) and from 180 to 240 per million (for children aged 15–19 years) (1, 5). Among the probable causes explaining the increase in children cancer incidence, the most often speculated are: the improvements in the diagnostics process, better cancer registration and changes in risk factors (5).

Three most common cancers among children are: leukaemia, lymphomas, and tumours of central nervous system. They constitute 70% of cancers in European children who are younger than 15 years and at the same time 50% of cancers in children aged 15–19 years (1, 5). Thanks to better understanding of cancers' morphology and advanced treatment modalities, the 5-year survival rates have improved, achieving the value of 80% (6, 7).

Oncological treatment includes chemotherapy, radiotherapy, surgery, or combination of different methods (8). Although, the above-mentioned treatment modalities are continuously being improved, they still have adverse impact on patients' future growth and development (9–14).

With the higher efficacy of children's oncologic treatment, the number of cancer survivors is increasing. As a consequence, more and more cancer survivors are seeking for orthodontic treatment. The knowledge about impact of previous oncological treatment on patients' facial growth, dental developmental abnormalities, and possible orthodontic treatment complications is absolutely necessary for orthodontists (15).

One of the most challenging things regarding the orthodontic treatment is its long-term stability (16). Only 30–50% of post-orthodontic patients presented satisfactory alignment of teeth 10 years after the end of the orthodontic treatment (17). It must be emphasized that retention, which aims to keep the teeth in their final position, is undoubtedly very important part of the orthodontic treatment (17, 18). Without orthodontic treatment stability, all other treatment goals, including ideal occlusal function and optimal aesthetics (both facial and dental) may be disturbed (18). Moreover, patients' treatment satisfaction becomes diminished when teeth return to their previous position (16). Both fixed and removable retainers are commonly used to reinforce the orthodontic treatment stability (19).

There are different indices used to assess the stability of the orthodontic treatment by comparing the occlusal anomalies at different stages of orthodontic treatment and during the follow-up period. There are two indices, which are most often used: the Peer Assessment Rating (PAR index) (20) and the Index of Complexity, Outcome and Need (ICON) (21).

Therefore, the aim of the study was to compare the stability of orthodontic treatment in cancer survivors treated with chemotherapy with a control group of healthy subjects.

Materials and methods

Study population

The study included 52 consecutive cancer survivor patients (29 males, 23 females; median age: 19.4; range: 13–28) who had received chemotherapy or chemotherapy combined with radiotherapy in their childhood because of cancer disease. These patients came to the specialist orthodontic practice, because they wanted to start orthodontic treatment. Primarily, the study sample consisted of 74 patients with oncologic history, but 22 patients were excluded: 2 patients were excluded due to poor oral hygiene, 13 patients did not come to the orthodontic practice during the retention period (maintenance therapy), and 7 patients did not come to the orthodontic practice during follow-up (after the retention period had been completed). Only the cancer survivors who had been treated during their childhood with chemotherapy or chemotherapy combined with radiotherapy were included into the study. The exclusion criteria were: previous orthodontic treatment, severe dentofacial deformities, such as cleft lip and palate, poor periodontal health, mental

health disorders, and patients who did not agree to take part into the study (22).

The control group consisted of generally healthy 52 patients (29 males, 23 females; median age: 19.8; range: 15–28) who were precisely matched for age (± 4 years), gender, malocclusion, and treatment time. None of the patients had ever been treated orthodontically. All of the participants of the control group were generally healthy, without any oncological history, without any chronic diseases and with no regular drug intake.

The indications for orthodontic treatment included: disturbances of the facial balance due to malocclusion, sagittal, transversal, and vertical discrepancies within and between the dental arches, teeth malalignment, crowding, and midlines discrepancies. The treatment objectives were: facial balance improvement, Class I canine and full class molar (preferably Class I molar, but also Class II molar in cases with Class II malocclusion, treated with extractions of teeth no: 14.24), correction of overbite and overjet to the recommended values, elimination of the crowding, aligning of the teeth in both arches, correction of midline discrepancies, and finally achievement of proper functional occlusion, including canine guidance and anterior guidance without posterior interferences.

The flow chart of participation is presented in Figure 1. Table 1 presents the general characteristics of cancer survivors' and control groups.

All of the cancer survivor patients were treated with chemotherapy and most of them suffered from leukaemia. Two patients had concomitant radiotherapy, but the area of head and neck was not irradiated. None of the examined patients had been treated with either immunotherapy or stem cells transplantation. The youngest patient diagnosed with cancer was under 1 year old and the oldest patient diagnosed with cancer was 7 years old. Supplementary Table 1 presents the general characteristics of the cancer survivors' group, including the type of the cancer, mean age at diagnosis, follow-up time, and treatment modality.

The detailed list of drugs used during chemotherapy in the cancer survivors' group included: antimetabolites (methotrexate, fluorouracil, cytarabine), antitumour antibiotics (doxorubicin, mitomycin, bleomycin), and plant alkaloids (vincristine, vinblastine, etoposide).

The study was approved by The Medical Board Ethical Committee (50/KBL/OIL/2010) and was conducted with the ethical principles of the World Medical Association Declaration of Helsinki. All of the patients and their parents received and signed informed consent.

Study protocol

Patients from both groups (examined and control ones) were recruited and treated orthodontically in the same specialist orthodontic private practice in Krakow (Poland). All patients were treated orthodontically between 2008 and 2013. The same as in our previous study (22), the process of orthodontic diagnosis was performed by two independent certified specialists of orthodontics, whereas the orthodontic treatment was performed by the certified specialist of orthodontics with 18 years of experience in the field of orthodontics (22).

The process of orthodontic diagnosis performed in both groups included: anamnesis, extraoral and intraoral orthodontic examination, analysis of plaster casts, analysis of extraoral and intraoral photographs, and analysis X-rays, including dental panoramic tomograms and lateral cephalograms. There were no patients in both groups diagnosed with either aberrations in root development or with jaw cysts.

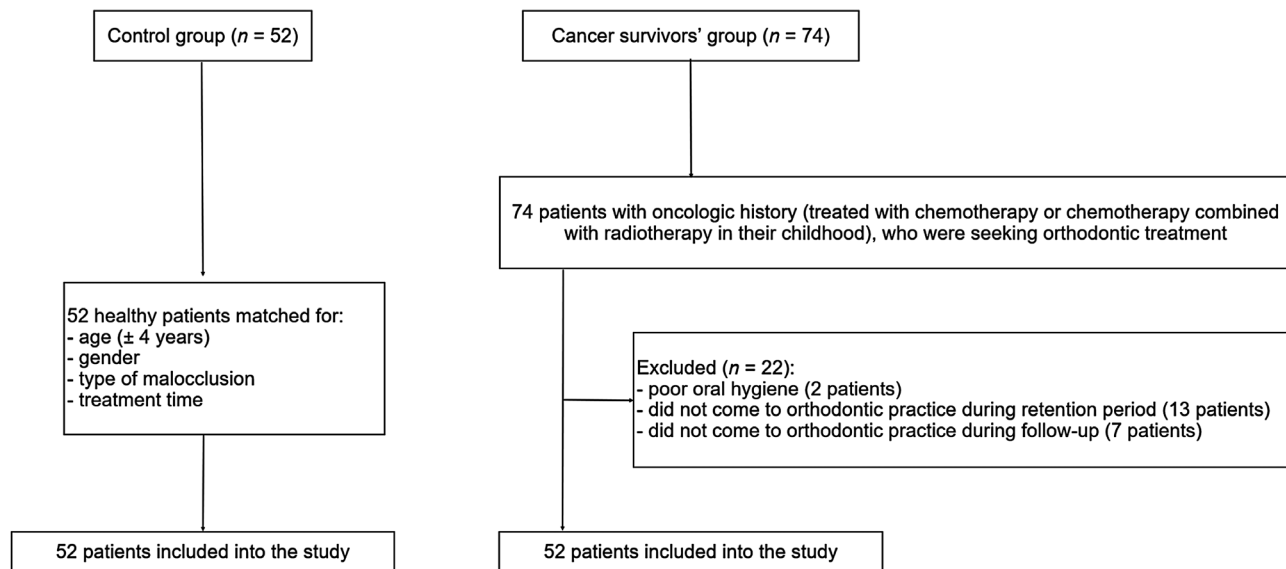


Figure 1. The flow chart of participation diagram.

Table 1. General characteristics of cancer survivors' and control group of patients.

| Factor | Cancer survivors' group | Control group | P-Value* | |
|---|-------------------------|-----------------|-----------------|-------|
| Number of patients (n) (female/male ratio) | 52 (23/29) | 52 (23/29) | 1.000 | |
| Median age (range) (years) | 19.4 (13–28) | 19.8 (15–28) | 0.821 | |
| Orthodontic assessment (the same for both groups) | Skeletal Class I | 13 | 13 | 1.000 |
| | | Low-angle—0 | Low-angle—0 | |
| | | Normal-angle—13 | Normal-angle—13 | |
| | Skeletal Class II | 33 | 33 | |
| | | Low-angle—4 | Low-angle—4 | |
| | | Normal-angle—29 | Normal-angle—29 | |
| | Skeletal Class III | 6 | 6 | |
| | | Low-angle—0 | Low-angle—0 | |
| | | Normal-angle—5 | Normal-angle—5 | |
| | | High-angle—1 | High-angle—1 | |

*U Mann–Whitney test.

On the basis of the diagnostics process, the treatment plans were prepared and the patients were classified to start the orthodontic treatment. One hundred and four patients (52 patients in each group) were treated with the vestibular fixed appliances (0.022-inch bracket slot, MBT prescription). The orthodontic treatment modalities in both groups are presented in [Supplementary Table 2](#).

All of the patients from both groups ended the orthodontic treatment with ideal occlusion according to six keys to normal occlusion by Andrews (23). All of the cases were treated with sliding mechanics. Goshgarian transpalatal bar and intermaxillary elastics were used to increase the anchorage. None of the cases needed skeletal anchorage devices to finish the treatment with the ideal occlusion.

After the active phase of the orthodontic treatment had been completed, the retention phase started. Retention protocol was exactly the same in both groups. All of the patients received lower lingual fixed retainer (bonded to all lower six front teeth from 33 to 43) and upper lingual fixed retainer (bonded to all upper six front teeth from 13 to 23) combined with upper removable Hawley retainer. All of the participants in both groups were told to wear Hawley appliance

night-time only (approximately 8 hours during a 24-hour cycle) for 1.5 years. Upper and lower fixed retainers were supposed to stay for a lifetime, but only in patients with good oral hygiene. The examined patients in both groups presented good oral hygiene, therefore there was no need to remove the fixed retainers. Patients' compliance with removable retainers was assessed by the usage of indirect methods, including questioning parents and patients, as well as by checking the appliances' fit. Patients' compliance was similar in both groups. Check-ups within the retention period were performed each 3 months for 1.5 years after the appliances had been removed.

The primary endpoint was to assess the stability of orthodontic treatment comparing the weighted Peer Assessment Rating Index (w-PAR index) (20) and the ICON index (21) before orthodontic treatment, immediately after orthodontic treatment, and at 3-year follow-up after orthodontic treatment. The value of the ICON index was also used for the assessment of the orthodontic treatment complexity as well as for the assessment the improvement grade (21).

[Supplementary Figure 1](#) presents our own examination card used for w-PAR index assessment, based on the Richmond *et al.* article

Table 2. The mean w-PAR index values before orthodontic treatment, after orthodontic treatment, and at 3-year follow-up in cancer survivors' and control groups.

| Measurement | Cancer survivors' group | Control group | P-Value* |
|------------------------------|---|---|----------|
| | Mean w-PAR index value \pm SD (range) | Mean w-PAR index value \pm SD (range) | |
| Before orthodontic treatment | 23.0 \pm 7.5 (4–40) | 22.6 \pm 6.2 (11–42) | 0.566 |
| After orthodontic treatment | 4.6 \pm 2.1 (0–8) | 4.2 \pm 1.9 (0–7) | 0.612 |
| At 3-year follow-up | 6.4 \pm 2.4 (2–12) | 4.9 \pm 2.1 (0–10) | 0.007 |

ANOVA, analysis of variance; w-PAR, weighted Peer Assessment Rating.
*ANOVA.

(20). **Supplementary Figure 2** presents the ICON index scoring method, based on the Daniels *et al.* article (21).

The secondary endpoint was to assess patients' satisfaction with the received orthodontic treatment. Treatment satisfaction was assessed using a validated 18-item questionnaire, containing 7 questions concerning dentofacial aesthetics, 6 questions concerning oral function, and 5 questions regarding psychosocial benefits of orthodontic treatment. Each question was evaluated by the patient in the 5-point Likert scale ranging from 1 (very dissatisfied) to 5 (very satisfied). The total score ranges from 16 (lowest satisfaction) to 80 (highest satisfaction). Questions number 3 and 5 were not scored. **Supplementary Table 3** presents the list of questions in the questionnaire regarding patients' satisfaction with orthodontic treatment (24).

Supplementary Figure 3 presents the study timeline. The w-PAR and ICON indices were assessed before orthodontic treatment, immediately after orthodontic treatment, and at 3-year follow-up. Whereas, patients' satisfaction with the received orthodontic treatment was assessed twice: immediately after the end of orthodontic treatment and at 3-year follow-up.

Statistical analysis

The data were analysed using Statistica 13.0 software (Dell Inc., Aliso Viejo, California, USA). No data were missing. Categorical variables were described as percentages of the total population, while continuous variables were reported as median and range. The nonparametric *U* Mann–Whitney test was used for comparisons. The analysis of variance test with repeated responses was used to assess the statistical significance between the scores. Statistical significance was set at $P \leq 0.05$.

Results

We calculated the required sample size considering the results of a pilot group, 90% of power and type I error 0.05. To detect 20% difference between the groups in the PAR in the ICON index after 3-year follow-up, the study sample in each group should include at least 49 patients.

More than half of the examined cancer survivors had been diagnosed with leukaemia (53.8%). The incidence of other types of cancers among the cancer survivors presented as follows: neuroblastoma (7.7%), soft tissue sarcoma (7.7%), non-Hodgkin's lymphoma (15.4%), and Wilms tumour (15.4%).

Skeletal Class I malocclusion was diagnosed in 13 patients (25%) in each group, skeletal Class II was diagnosed in 33 patients (63.5%) in each group and skeletal Class III was diagnosed in 6 patients (11.5%) in each group. Both groups (the cancer survivors' and the control ones) were perfectly matched for the type of malocclusion. The mean follow-up time was 36.4 months in both groups. Although, the mean treatment time was shorter in the cancer survivors' group comparing to the control group, the difference was not statistically significant (17.6 versus 18.1 months; $P > 0.05$).

None of the cancer survivors had been diagnosed both clinically and radiographically with any of the dental morphology disturbances due to the previously received chemotherapy or chemotherapy combined with radiotherapy.

Pre-treatment index assessment of complexity

According to the values of the ICON index, the complexity of the orthodontic treatment among 50% of the cancer survivors and 50% of the control group were graded as moderate. Moreover, 36.5% of cancer survivors' cases and 38.5% of control group's cases were graded as difficult and very difficult. **Supplementary Table 4** presents treatment complexity grades on the basis of the ICON index value in both groups. There were no statistically significant differences between the groups regarding the complexity grade assessed on the basis of the ICON index value.

The weighted PAR index

An appropriate ideal occlusion was achieved in all patients with the mean w-PAR index of 4.6 in the cancer survivors' group and 4.2 in the control group. The differences between the w-PAR index before and after the treatment were statistically insignificant between these two groups. However, at 3-year follow-up, the mean w-PAR index was significantly higher in the cancer survivors' group comparing to the control group ($P = 0.007$). **Table 2** and **Figure 2** present mean w-PAR index values before orthodontic treatment, after orthodontic treatment, and at 3-year follow-up.

There was a significant decrease in the mean w-PAR index value after orthodontic treatment and at 3-year follow-up comparing to the value measured before the onset of the orthodontic treatment in both groups ($P < 0.001$). Although the mean w-PAR index value reduction was higher in the control group, the difference between the groups was not significant ($P = 0.723$).

Moreover, in the cancer survivors' group there was a statistically significant increase in the mean w-PAR index value at 3-year follow-up comparing to the value measured immediately after the end of the orthodontic treatment ($P < 0.001$). There was also an increase in the mean w-PAR index value at 3-year follow-up comparing to the value measured immediately after the end of the orthodontic treatment in the control group, but this change was statistically insignificant. **Table 3** presents the mean w-PAR index changes between different measurements within and between the examined groups.

The ICON index

After orthodontic treatment the mean ICON index values were reduced from 62.4 to 10.2 for the cancer survivors and from 64.0 to 9.3 for the control group. There were no statistically significant differences between the examined groups regarding the mean ICON index values before and after orthodontic treatment. However, the mean ICON index value at 3-year follow-up in cancer survivors was significantly higher comparing to the control group ($P = 0.004$).

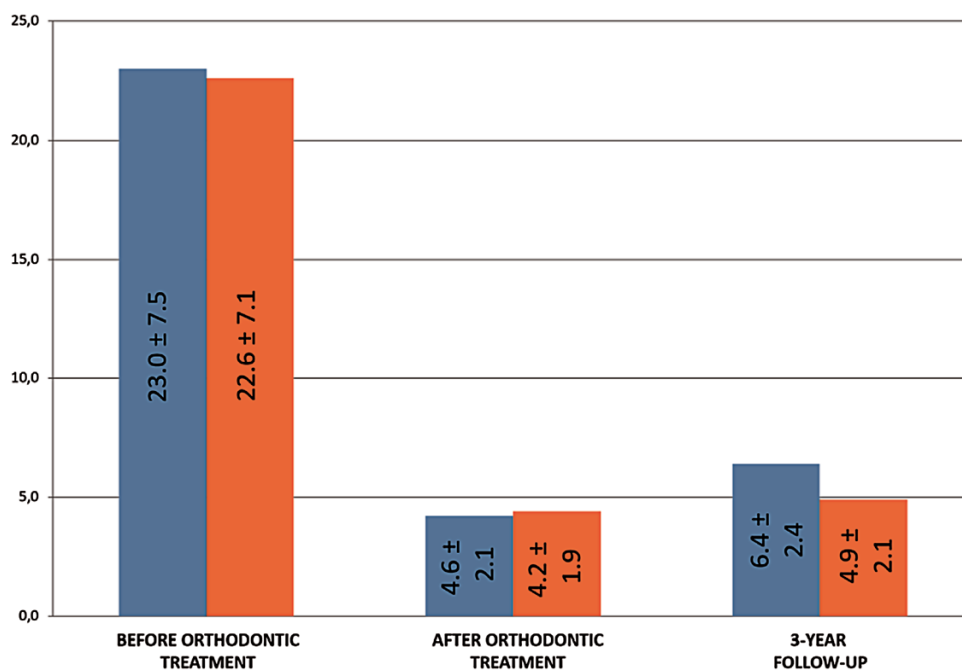


Figure 2. The bar chart presenting mean w-PAR index values before orthodontic treatment, after orthodontic treatment, and at 3-year follow-up in cancer survivors' (blue) and control (red) groups. w-PAR, weighted Peer Assessment Rating.

Table 3. The mean w-PAR index changes between different measurements within the examined groups and between them.

| Compared measurements | Cancer survivors' group | Control group | P-Value* |
|--|-----------------------------------|-----------------------------------|----------|
| | Mean w-PAR change | Mean w-PAR change | |
| Before versus after orthodontic treatment | Reduction 80.0% ($P < 0.001^*$) | Reduction 81.4% ($P < 0.001^*$) | 0.723* |
| Before orthodontic treatment versus 3-year follow-up | Reduction 72.2% ($P < 0.001^*$) | Reduction 78.3% ($P < 0.001^*$) | 0.422* |
| After orthodontic treatment versus 3-year follow-up | Increase 39.1% ($P < 0.001^*$) | Increase 16.7% ($P = 0.082^*$) | <0.001* |

w-PAR, weighted Peer Assessment Rating.

*U Mann-Whitney test.

Table 4 presents the mean ICON index values before orthodontic treatment, after orthodontic treatment, and at 3-year follow-up.

There was a significant decrease in the mean ICON index value after orthodontic treatment and at 3-year follow-up comparing to the value measured before the onset of the orthodontic treatment in both groups ($P < 0.001$). Although the mean ICON index value reduction was higher in control group, the difference between the groups was not significant ($P = 0.651$ and $P = 0.106$, respectively). In the cancer survivors' group there was a statistically significant increase in the mean ICON index value at 3-year follow-up comparing to the value measured immediately after the end of the orthodontic treatment ($P < 0.001$). Although, there was also an increase in the mean ICON index value at 3-year follow-up comparing to the value measured immediately after the end of the orthodontic treatment in the control group, this change was statistically insignificant

Table 4. The mean ICON index values before orthodontic treatment, after orthodontic treatment, and at 3-year follow-up in cancer survivors' and control groups.

| Measurement | Cancer survivors' group | Control group | P-Value* |
|------------------------------|------------------------------------|------------------------------------|----------|
| | Mean ICON index value ± SD (range) | Mean ICON index value ± SD (range) | |
| Before orthodontic treatment | 62.4 ± 11.9 (40–96) | 64.0 ± 12.1 (42–97) | 0.617 |
| After orthodontic treatment | 10.2 ± 3.3 (7–14) | 9.3 ± 4.1 (7–14) | 0.542 |
| At 3-year follow-up | 15.6 ± 2.6 (7–26) | 10.2 ± 3.2 (7–16) | 0.004 |

ANOVA, analysis of variance; ICON, Index of Complexity, Outcome and Need.

*ANOVA.

($P = 0.241$). **Table 5** presents the mean ICON index changes between different measurements within and between the examined groups.

Assessment of the improvement grade at 3-year follow-up

Improvement grade was assessed on the basis of pre-treatment and post-treatment ICON index values with the formula: Improvement grade = pre-treatment score – 4 × post-treatment score (21). **Supplementary Table 5** presents the improvement grades at 3-year follow-up in the examined groups.

The Patients Satisfaction Score

Patients' satisfaction with the received orthodontic treatment decreased in both groups at 3-year follow-up comparing to the results

Table 5. The mean ICON index changes between different measurements within the examined groups and between them.

| Compared measurements | Cancer survivors' group | Control group | P-Value* |
|--|--------------------------------------|--------------------------------------|----------|
| | Mean ICON change | Mean ICON change | |
| Before versus after orthodontic treatment | Reduction 83.7% ($P < 0.001^*$) | Reduction 85.5% ($P < 0.001^*$) | 0.651* |
| Before orthodontic treatment versus 3-year follow-up | Reduction 75.2% ($P < 0.001^*$) | Reduction 84.1% ($P < 0.001^*$) | 0.106* |
| After orthodontic treatment versus 3-year follow-up | Increase 52.9% ($P < 0.001^*$) | Increase 9.7% ($P = 0.241^*$) | <0.001* |

ICON, Index of Complexity, Outcome and Need.

*U Mann–Whitney test.

obtained at the end of the orthodontic treatment. However, the differences were not statistically significant. [Supplementary Table 6](#) presents the median values of Patient Satisfaction Score immediately after orthodontic treatment and at 3-year follow-up in both groups.

Discussion

This study is the first one that analyses the stability of orthodontic treatment in cancer survivor patients and assesses cancer survivor patients' satisfaction with the received treatment. Moreover, these outcomes have been compared with the results obtained in the generally healthy patients who had been matched for age, gender, type of malocclusion, and time of treatment.

Orthodontic treatment of cancer survivor patients requires specific knowledge from the specialists of orthodontics. According to the research by Neill *et al.* (15), the majority of orthodontists did not receive adequate training to treat cancer survivors. Therefore, the authors suggested that the orthodontic education focussing on the treatment of cancer survivors should be widespread not only at the predoctoral, but also at the graduate levels.

Dental complications as consequences of previous oncological treatment

According to the literature, the vast majority of cancer survivors were diagnosed with at least one type of dental complication, including malaligned teeth, root stunting, growth and development changes, missing teeth, delay in loss of deciduous teeth, microdontia, and enamel hypoplasia (15, 25, 26). Moreover, chemotherapy was found to be related to premature apexification, arrested root development, and tooth discolouration, but also to worse oral hygiene, increased caries intensity, oral lesions, and hyposalivation (25). It has been summarized that both chemotherapy and radiotherapy have impact on the development of crown and roots of the teeth, while root defects occur more commonly (27). The most common root defect was impaired root growth, whereas the most common crown defect was microdontia (27). In addition to this, it cannot be distinguished that the defects in odontogenesis are caused either only by chemotherapy or radiotherapy, because modern oncological treatment modalities include both chemo- and radiotherapy (27, 28). Furthermore, it has been proven that the presence of dental abnormalities is associated

with the patients' age at the moment of oncological treatment. The highest risk of the development of dental abnormalities occurs when children receive anticancer treatment before the age of 5 years (27, 29, 30). Although the majority of our patients were diagnosed with oncological disease before turning 5 years old, we observed none of the abovementioned symptoms among our patients. The reason for that could have been: the limited number of cancer survivors included into the study and the fact that there were only 2 cancer survivors in our study who had received additional radiotherapy. Moreover, none of those two patients had been irradiated in the area of head and neck. Thus, these observations probably could have been different if the sample size of our study had been bigger and if the study sample had included more cancer survivors who had received combined methods of oncological treatment.

Guidelines for orthodontic treatment of cancer survivors

So far, there have been published several guidelines regarding the orthodontic treatment of cancer survivor patients receiving immunosuppressive therapy and/or radiation (31). The American Academy of Paediatric Dentistry recommends maintaining optimal oral health, amplification of optimal oral and dental care for life, as well as treatment of any dental diseases which could have arisen as a consequence of long-term effects of immunosuppressive therapy. Moreover, the orthodontic treatment in cancer survivors may be started not earlier than 2 years after recovery and only among survivors who do not take any immunosuppressive drugs. Orthodontists should choose appliances which reduce the risk of root resorption and create light forces. In addition to this, treatment time ought to be shortened, the chosen method of treatment must be as simple as possible to achieve the treatment needs and it is not recommended to treat the lower jaw (31, 32). The orthodontic treatment of cancer survivors included into our study was performed with the majority of the abovementioned principles. All of the participants started their treatment more than 2 years after recovery and none of them were taking any immunosuppressive drugs. Although, it is recommended to treat only upper arch, we decided to perform orthodontic treatment in all cases in both arches to finish the treatment with ideal occlusion. The mean treatment time was insignificantly shorter in the cancer survivors' group comparing to the control group.

Long-term stability of orthodontic treatment in cancer survivors

Despite the fact that the abovementioned suggestions are of great importance, so far nothing has been written about the stability of orthodontic treatment and the retention period in cancer survivors.

Long-term stability of the orthodontic treatment still remains one of the major problems of contemporary orthodontics. de Bernabé *et al.* (16) found that long-term stability (between 4 and 10 years after the end of orthodontic treatment) could have been described as absolute stability only in 7.1% of cases and as relative stability in 68.6% of cases. According to the authors the least stable occlusal features were: alignment of lower anterior segment and overbite. Littlewood *et al.* (33) analysed the aetiology of relapse after orthodontic treatment. They listed several factors which have impact on stability of orthodontic treatment, including: periodontal and gingival factors, occlusal factors, soft tissue pressures, and limits of the dentition, as well as factors leading to so-called physiological relapse (facial growth and age-related changes during the lifetime). In addition to this, Woods (34) emphasized the role of the

mandibular muscles in the long-term occlusal stability. According to our research, there was a significant worsening of the treatment stability during 3-year retention period among cancer survivors comparing to healthy subjects.

There can be listed several limitations to our study. Firstly, the examined group of cancer survivors consisted of only 52 people, treated in their childhood due to different types of tumours, both the solid tumours and the haematological malignancies. The limited size of the study sample as well as different types of oncological diagnoses could have had an impact on the final results of the study. Secondly, most of the participants included into the study were adolescents and young adults. Young population could be not representative for a whole population that survived a cancer treatment. Thirdly, although the examined groups were perfectly matched for the types of malocclusion, both of them included Class I, II, and III malocclusions. The stability of orthodontic treatment depends on the type of tooth movement which varies in different types of malocclusions. Fourthly, there were two more patients in the control group who had been treated orthodontically with extractions comparing to the cancer survivors' group. Orthodontic treatment with extractions could have had positive impact on treatment stability. Fifthly, the stability of orthodontic treatment may also depend on periodontal and gingival factors, as well as soft tissue pressure which were not measured quantitatively and compared between the two groups.

Conclusions

The results of properly conducted orthodontic treatment of cancer survivors did not differ significantly from the results obtained among generally healthy patients. However, there was a significant worsening of the treatment stability during 3-year retention period among cancer survivors comparing to healthy subjects. Therefore, cancer survivors need a more intense follow-up period to maintain the achieved results of orthodontic treatment. Moreover, cancer survivors should be informed, prior to the treatment, about higher risk of orthodontic relapse.

Supplementary material

Supplementary material is available at *European Journal of Orthodontics* online.

Supplementary Figure 1. Examination card used for weighted Peer Assessment Rating Index.

Supplementary Figure 2. Examination card used for Index of Complexity, Outcome and Need.

Supplementary Figure 3. The study timeline.

Supplementary Table 1. General characteristics of the cancer survivors' group, including the type of cancer, mean age at diagnosis, follow-up time, and treatment modality.

Supplementary Table 2. Orthodontic treatment modalities in cancer survivors' and control groups.

Supplementary Table 3. The list of questions in the questionnaire regarding patients' satisfaction with orthodontic treatment (24).

Supplementary Table 4. Complexity grades in cancer survivors' and control groups.

Supplementary Table 5. Improvement grade at 3-year follow-up in cancer survivors' and control groups.

Supplementary Table 6. The median values of Patient Satisfaction Score after orthodontic treatment and at 3-year follow-up in cancer survivors' and control groups.

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This research received no external funding.

Conflicts of interest

None to declare.

Data availability

The data underlying this article are available in the article and in its online supplementary material.

References

1. Steliarova-Foucher, E., Colombet, M., Ries, L.A.G., Moreno, F., Dolya, A., Bray, F., Hesselting, P., Shin, H.Y. and Stiller, C.A.; IICC-3 contributors. (2017) International incidence of childhood cancer, 2001–10: a population-based registry study. *The Lancet Oncology*, 18, 719–731.
2. Reedijk, A.M.J., Kremer, L.C., Visser, O., Lemmens, V., Pieters, R., Coebergh, J.W.W. and Karim-Kos, H.E. (2020) Increasing incidence of cancer and stage migration towards advanced disease in children and young adolescents in the Netherlands, 1990–2017. *European Journal of Cancer (Oxford, England: 1990)*, 134, 115–126.
3. Sommer, G., Schindler, M., Redmond, S., Pfeiffer, V., Konstantinou, G., Ammann, R.A., Ansari, M., Hengartner, H., Michel, G. and Kuehni, C.E.; Swiss Paediatric Oncology Group (SPOG). (2019) Temporal trends in incidence of childhood cancer in Switzerland, 1985–2014. *Cancer Epidemiology*, 61, 157–164.
4. Jastaniah, W., Essa, M.F., Ballourah, W., Abosoudah, I., Al Daama, S., Algiraigri, A.H., Al Ghemlas, I., Alshahrani, M. and Alsultan, A. (2020) Incidence trends of childhood acute lymphoblastic leukemia in Saudi Arabia: increasing incidence or competing risks? *Cancer Epidemiology*, 67, 101764.
5. Steliarova-Foucher, E., et al.; ACCIS contributors. (2018) Changing geographical patterns and trends in cancer incidence in children and adolescents in Europe, 1991–2010 (Automated Childhood Cancer Information System): a population-based study. *The Lancet Oncology*, 19, 1159–1169.
6. Gatta, G., et al.; EURO CARE Working Group. (2014) Childhood cancer survival in Europe 1999–2007: results of EURO CARE-5—a population-based study. *The Lancet Oncology*, 15, 35–47.
7. Erdmann, F., Frederiksen, L.E., Bonaventure, A., Mader, L., Hasle, H., Robison, L.L. and Winther, J.F. (2020) Childhood cancer: survival, treatment modalities, late effects and improvements over time. *Cancer Epidemiology*, 101733. First published on May 24, 2020.
8. Knighting, K., Kirton, J.A., Thorp, N., Hayden, J., Appleton, L. and Bray, L. (2020) A study of childhood cancer survivors' engagement with long-term follow-up care: 'to attend or not to attend, that is the question'. *European Journal of Oncology Nursing*, 45, 101728.
9. Paulino, A.C., Simon, J.H., Zhen, W. and Wen, B.C. (2000) Long-term effects in children treated with radiotherapy for head and neck rhabdomyosarcoma. *International Journal of Radiation Oncology, Biology, Physics*, 48, 1489–1495.
10. Mishra, S.K., Chowdhary, R. and Kumari, S. (2017) Microleakage at the different implant abutment interface: a systematic review. *Journal of Clinical and Diagnostic Research*, 11, ZE10–ZE15.
11. Bruzzi, P., Bigi, E., Predieri, B., Bonvicini, F., Cenciarelli, V., Felici, F. and Iughetti, L. (2019) Long-term effects on growth, development, and metabolism of ALL treatment in childhood. *Expert Review of Endocrinology & Metabolism*, 14, 49–61.
12. Elitzur, S., et al. (2017) Growth and pubertal patterns in young survivors of childhood acute lymphoblastic leukemia. *Journal of Pediatric Endocrinology & Metabolism*, 30, 869–877.
13. Kaste, S.C., et al. (2009) Impact of radiation and chemotherapy on risk of dental abnormalities: a report from the Childhood Cancer Survivor Study. *Cancer*, 115, 5817–5827.

14. Nemeth, O., Hermann, P., Kivovics, P. and Garami, M. (2013) Long-term effects of chemotherapy on dental status of children cancer survivors. *Pediatric Hematology and Oncology*, 30, 208–215.
15. Neill, C.C., Migliorati, C., Trojan, T., Kaste, S., Karydis, A., Rowland, C. and Parris, W. (2015) Experience and expertise regarding orthodontic management of childhood and adolescent cancer survivors. *American Journal of Orthodontics and Dentofacial Orthopedics*, 148, 765–770.
16. de Bernabé, P.G., Montiel-Company, J.M., Paredes-Gallardo, V., Gandía-Franco, J.L. and Bellot-Arcís, C. (2017) Orthodontic treatment stability predictors: a retrospective longitudinal study. *The Angle Orthodontist*, 87, 223–229.
17. Yu, Y., Sun, J., Lai, W., Wu, T., Koshy, S. and Shi, Z. (2013) Interventions for managing relapse of the lower front teeth after orthodontic treatment. *Cochrane Database of Systematic Reviews*, 6, 1–20.
18. Joondeph, D.R., Huang, G. and Little, R. (2017) Stability, retention, and relapse. In Graber, L.W., Vanarsdall, R.L., Vig, K.W.L. and Huang, G.J. (eds.), *Orthodontics Current Principles and Techniques*. Elsevier, St. Louis, MO, Vol. 1, 6th edn, pp. 981–995.
19. Johnston, C.D. and Littlewood, S.J. (2015) Retention in orthodontics. *British Dental Journal*, 218, 119–122.
20. Richmond, S., Shaw, W.C., O'Brien, K.D., Buchanan, I.B., Jones, R., Stephens, C.D., Roberts, C.T. and Andrews, M. (1992) The development of the PAR Index (Peer Assessment Rating): reliability and validity. *European Journal of Orthodontics*, 14, 125–139.
21. Daniels, C. and Richmond, S. (2000) The development of the index of complexity, outcome and need (ICON). *Journal of Orthodontics*, 27, 149–162.
22. Mitus-Kenig, M., Derwich, M., Czochrowska, E. and Pawlowska, E. (2020) Quality of life in orthodontic cancer survivor patients—a prospective case-control study. *International Journal of Environmental Research and Public Health*, 17, E5824.
23. Andrews, L.F. (1972) The six keys to normal occlusion. *American Journal of Orthodontics*, 62, 296–309.
24. Uslu, O. and Akcam, M.O. (2007) Evaluation of long-term satisfaction with orthodontic treatment for skeletal class III individuals. *Journal of Oral Science*, 49, 31–39.
25. Busenhardt, D.M., Erb, J., Rigakos, G., Eliades, T. and Papageorgiou, S.N. (2018) Adverse effects of chemotherapy on the teeth and surrounding tissues of children with cancer: a systematic review with meta-analysis. *Oral Oncology*, 83, 64–72.
26. Proc, P., Szczepańska, J., Skiba, A., Zubowska, M., Fendler, W. and Młynarski, W. (2016) Dental anomalies as late adverse effect among young children treated for cancer. *Cancer Research and Treatment*, 48, 658–667.
27. Seremidi, K., Kloukos, D., Polychronopoulou, A., Kattamis, A. and Kavvadia, K. (2019) Late effects of chemo and radiation treatment on dental structures of childhood cancer survivors. A systematic review and meta-analysis. *Head & Neck*, 41, 3422–3433.
28. Psoter, W.J. and Shope, E.T. (2019) Some cancer chemotherapy (CH) agents may be associated with tooth agenesis, though CH dose, age of CH exposure, and dental development at the time of treatment may be critical determinants. *The Journal of Evidence-Based Dental Practice*, 19, 101352.
29. Hernandez, M., Pochon, C., Chastagner, P. and Droz, D. (2019) Long-term adverse effects of acute myeloid leukemia treatment on odontogenesis in a child. *International Journal of Clinical Pediatric Dentistry*, 12, 243–246.
30. Çetiner, D., Çetiner, S., Uraz, A., Alpaslan, G.H., Alpaslan, C., Toygar Memikoğlu, T.U. and Karadeniz, C. (2019) Oral and dental alterations and growth disruption following chemotherapy in long-term survivors of childhood malignancies. *Supportive Care in Cancer*, 27, 1891–1899.
31. Dental management of pediatric patients receiving immunosuppressive therapy and/or radiation therapy. (2018) *Pediatric Dentistry*, 40, 392–400.
32. Dahllöf, G. and Huggare, J. (2004) Orthodontic considerations in the pediatric cancer patient: a review. *Seminars in Orthodontics*, 10, 266–276.
33. Littlewood, S.J., Kandasamy, S. and Huang, G. (2017) Retention and relapse in clinical practice. *Australian Dental Journal*, 62(Suppl 1), 51–57.
34. Woods, M.G. (2017) The mandibular muscles in contemporary orthodontic practice: a review. *Australian Dental Journal*, 62(Suppl 1), 78–85.