**Appositional bone growth is a risk for aseptic loosening following lower extremity endoprosthetic reconstruction in pediatric bone sarcoma patients**

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**Abstract**

Significance & Hypothesis

Endoprosthetic reconstruction is a common limb-salvage technique in pediatric bone sarcoma when the physis cannot be spared. Aseptic loosening (AL) is a known complication after endoprosthesis and has been associated with the diaphyseal:stem ratio. While previous reports have described the incidence of AL in pediatric patients, the underlying causes remain largely uninvestigated. Skeletal growth in these patients is difficult to predict, and the impact of appositional growth on stem stability is unclear. The purpose of this study was to determine if appositional bone growth around an endoprosthetic stem is associated with AL in pediatric patients. We hypothesize that greater appositional bone growth will produce higher rates of AL.

Innovation

The concept of appositional bone growth affecting the stability of stemmed endoprostheses in children has not been investigated in the literature and represents a novel analysis.

Approach

A single-center retrospective cohort study was conducted on 78 patients <18 years old who underwent a lower extremity endoprosthetic reconstruction for sarcoma with >6 months follow-up. Patients were stratified into two groups: patients with AL (n=13) and without AL (n=65). Diagnosis of AL was based on weight bearing pain and/or radiographic stem migration/subsidence, progressive radiolucency around the stem, or fractured cement mantle. Calibrated measurements were compared between the first postoperative radiograph (TP1) and the radiograph at most recent follow-up (TP2), or at the time of aseptic loosening diagnosis (TP loosening). Measurements were taken at 60% of the length of the endoprosthetic stem, and growth indices were calculated including the periosteal-stem index (PSI), endosteal-stem index (ESI), and cortical-stem index (CSI) (Figure 1). Outcomes of patients who were skeletally immature versus those nearing skeletal maturity were compared (based on radiographic appearance of the ipsilateral non-instrumented long bone physis).

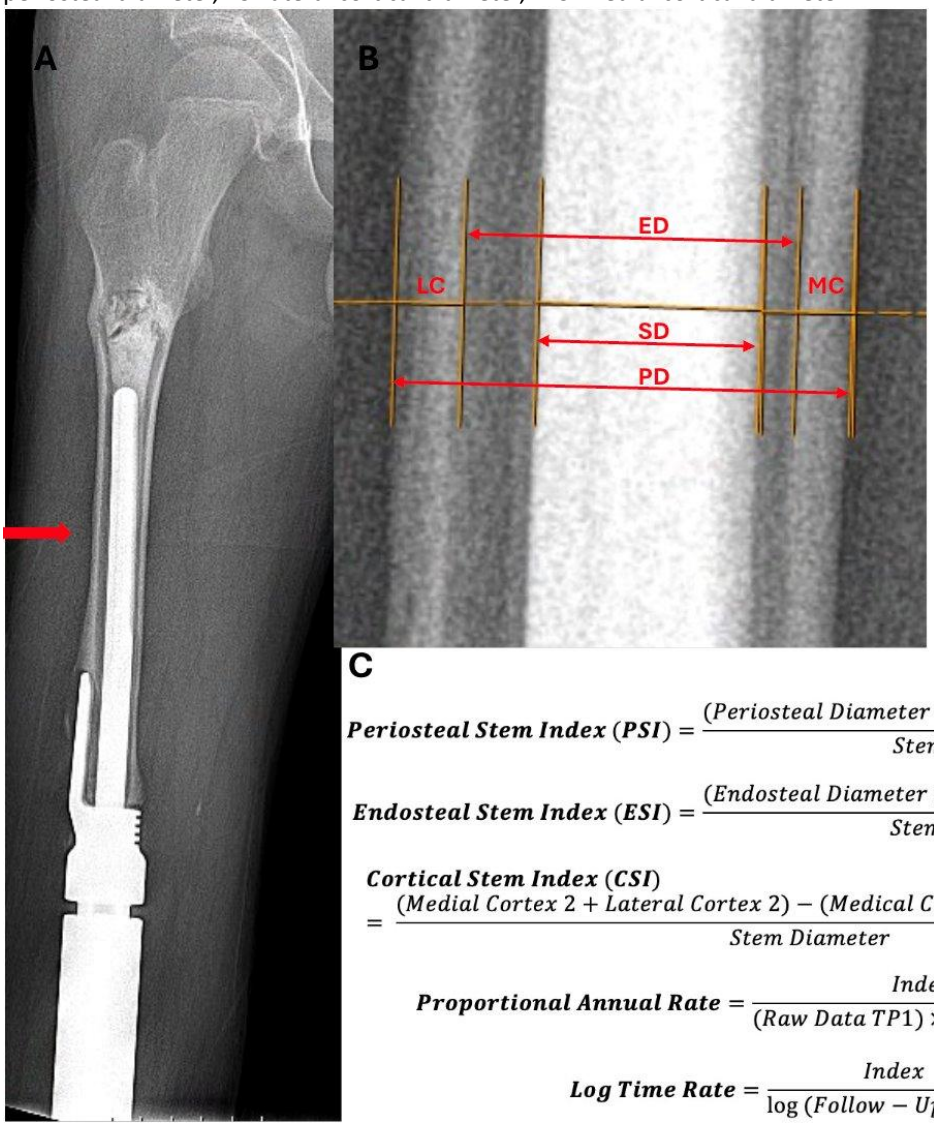
Results

The overall rate of AL was 17% (13/78) at median follow-up of 3 years (IQR 1.23-5.07). There were no baseline differences between patients with and without AL including the use of cement (69% AL vs. 57% no AL, p=0.542), expandible prostheses (39% AL vs. 29% no AL, p=0.517), collar type (p=0.577), and side plate (31% AL vs. 13% no AL, p=0.112) (Table I). Patients with AL showed more appositional growth over time with larger PSI [log-time rate: 0.26 vs. 0.05 (p=0.015)], and larger ESI [log-time rate: 0.35 vs. 0.04 (p<0.001); proportional annual rate: 7.29 vs 1.09 (p=0.009)]. The CSI declined over time and was similar between groups [proportional annual rate: -5.84 vs.-0.69 (p=0.43)]. The rate of AL in skeletally immature patients was higher than those nearing skeletal maturity (23% (12/53) vs. 4% (1/25), p=0.049). Among skeletally immature patients, those with AL showed more appositional bone growth with larger ESI [log-time rate: 0.43 vs. 0.05 (p=0.003); proportional annual rate: 9.27 vs. 1.02 (p=0.008)] and a trend toward larger PSI [proportional annual rate: 2.99 vs. 0.3 (p=0.054)] (Table II).

Discussion & Impact

Aseptic loosening of lower extremity endoprostheses in pediatric sarcoma is associated with increased appositional growth of the bone around the stem due to increased periosteal diameter, endosteal widening and decreased cortical thickness.

**Figure 1:** (A) AP x-ray of a 13 year old male with a cemented noninvasive expandible endoprosthesis with aseptic loosening. The *red arrow* depicts the standardized location for the bone measurements, corresponding to 60% of the total stem length. (B) Depiction of the standardized bone measurements. (C) Formulas used to calculate the proportional annual rate and log-time rate of the growth indices. ED: endosteal diameter, SD: stem diameter, PD: periosteal diameter, LC: lateral cortical diameter, MC: medial cortical diameter.




C

$$\textbf{Periosteal Stem Index (PSI)} = \frac{(Periosteal\ Diameter\ 2) - (Periosteal\ Diameter\ 1)}{Stem\ Diameter}$$

$$\textbf{Endosteal Stem Index (ESI)} = \frac{(Endosteal\ Diameter\ 2) - (Endosteal\ Diameter\ 1)}{Stem\ Diameter}$$

$$\textbf{Cortical Stem Index (CSI)} = \frac{(Medial\ Cortex\ 2 + Lateral\ Cortex\ 2) - (Medical\ Cortex\ 1 + Lateral\ Cortex\ 1)}{Stem\ Diameter}$$

$$\textbf{Proportional Annual Rate} = \frac{Index \times 100}{(Raw\ Data\ TP1) \times (Follow - Up\ Years)}$$

$$\textbf{Log Time Rate} = \frac{Index}{\log (Follow - Up\ Years)}$$

**Table I.** Patient baseline characteristics by loosening status.

| Variable | All (n=78) | Aseptic Loosening (n=13) | No Aseptic Loosening (n=65) | p-value |
|---|---|---|---|---|
| **N** | **78** | **13** | **65** | |
| ***Demographic Information*** | | | | |
| Age at surgery, years; median (range) | 13.91 (7.2-17.9–16.4) | 13.05 (9.3-17.8) | 14.27 (7.2–17.9) | 0.283 |
| Female sex; n (%) | 31 (39.7%) | 6 (46.2%) | 25 (38.5%) | 0.758 |
| BMI, kg/m²; median (IQR) | 19.34 (17.17–23.42) | 20.32 (16.03–31.26) | 19.25 (17.38–21.63) | 0.677 |
| Weight, kg; median (IQR) | 55.45 (41.92–67.7) | 51.45 (37.1–86.8) | 55.45 (42.9–66.1) | 0.94 |
| Skeletally immature at surgery; n (%) | 53 (67.9%) | 12 (92.3%) | 41 (63.1%) | 0.051 |
| Follow-up duration, years; median (IQR) | 2.99 (1.23–5.07) | 3.18 (2.11–4.43) | 2.77 (1.07–5.24) | 0.471 |
| ***Oncologic Factors*** | | | | |
| Known metastatic disease; n (%) | 16 (20.5%) | 2 (15.4%) | 14 (21.5%) | 1 |
| Neoadjuvant chemotherapy; n (%) | 76 (97.4%) | 12 (92.3%) | 64 (98.5%) | 0.307 |
| Adjuvant chemotherapy; n (%) | 61 (78.2%) | 8 (61.5%) | 53 (81.5%) | 0.143 |
| Neoadjuvant radiation; n (%) | 0 (0%) | 0 (0%) | 0 (0%) | — |
| Adjuvant radiation; n (%) | 1 (1.3%) | 0 (0%) | 1 (1.5%) | 1 |
| Tumor size at resection, mm; median (IQR) | 8.9 (6.8–14) | 9.6 (7.2–12.15) | 8.8 (6.8–14) | 0.932 |
| ***Surgical Factors*** | | | | |
| Anatomic location | | | | 0.329 |
| Proximal femur; n (%) | 14 (17.9%) | 1 (7.7%) | 13 (20%) | |
| Distal femur; n (%) | 44 (56.4%) | 10 (76.9%) | 34 (52.3%) | |
| Proximal tibia; n (%) | 20 (25.6%) | 2 (15.4%) | 18 (27.7%) | |
| Length of bony resection, mm; median (IQR) | 170 (141.25–190) | 180 (165–200) | 165 (140–190) | 0.186 |
| Stem type | | | | 0.762 |
| Curved; n (%) | 34 (44.7%) | 5 (38.5%) | 29 (46%) | |
| Straight; n (%) | 42 (55.3%) | 8 (61.5%) | 34 (54%) | |
| Cemented stem; n (%) | 46 (59%) | 9 (69.2%) | 37 (56.9%) | 0.542 |
| Prosthesis type | | | | 0.517 |
| Lengthening; n (%) | 23 (30.3%) | 5 (38.5%) | 18 (28.6%) | |
| Static; n (%) | 53 (69.7%) | 8 (61.5%) | 45 (71.4%) | |
| Stem Diameter, Zone 3, mm (IQR) | 10.95 (9–12.5) | 9.3 (8.5–12) | 11 (9–12.5) | 0.49 |
| Stem Length, mm (IQR) | 127 (104–150) | 125 (100–137) | 127 (112–150) | 0.434 |
| Collar type | | | | 0.577 |

| Variable | All (n=78) | Aseptic Loosening (n=13) | No Aseptic Loosening (n=65) | p-value |
|---|---|---|---|---|
| HA coated; n (%) | 17 (22.1%) | 4 (30.8%) | 13 (20.3%) | |
| Polished metal; n (%) | 55 (71.4%) | 9 (69.2%) | 46 (71.9%) | |
| Porous metal coated; n (%) | 5 (6.5%) | 0 (0%) | 5 (7.8%) | |
| Side plate; n (%) | 12 (15.6%) | 4 (30.8%) | 8 (12.5%) | 0.112 |
| Prior infection; n (%) | 1 (1.3%) | 0 (0%) | 1 (1.5%) | 1 |
| Prior surgery at site; n (%) | 16 (20.5%) | 4 (30.8%) | 12 (18.5%) | 0.45 |

Continuous variables: median (IQR), compared using Mann-Whitney U test. Categorical variables: n (%), compared using Fisher's exact test. HA = hydroxyapatite.

**Table II.** Appositional growth indices by loosening status.

| Variable | All Patients (n=78) | Aseptic Loosening (n=13) | No Aseptic Loosening (n=65) | p-value |
|---|---|---|---|---|
| **N** | **78** | **13** | **65** | |
| ***Periosteal-Stem Index (PSI)*** | | | | |
| Proportional annual rate; median (IQR) | 0.56 (-0.22–2.69) | 2.65 (0.56–5.96) | 0.35 (-0.32–1.81) | 0.06 |
| Log-time rate; median (IQR) | 0.09 (0–0.23) | 0.26 (0.1–0.59) | 0.05 (0–0.17) | 0.015* |
| ***Endosteal-Stem Index (ESI)*** | | | | |
| Proportional annual rate; median (IQR) | 1.44 (-0.06–5.78) | 7.29 (3.5–14.47) | 1.09 (-0.37–3.19) | 0.009* |
| Log-time rate; median (IQR) | 0.06 (0–0.22) | 0.35 (0.25–0.61) | 0.04 (-0.02–0.1) | <0.001* |
| ***Cortical-Stem Index (CSI)*** | | | | |
| Proportional annual rate; median (IQR) | -1.01 (-6.85–2.92) | -5.84 (-12.52–3.86) | -0.69 (-6.4–2.66) | 0.429 |
| Log-time rate; median (IQR) | 0.01 (-0.09–0.11) | -0.1 (-0.25–0.09) | 0.01 (-0.07–0.11) | 0.26 |
| **Variable** | **Skeletally Immature Patients (n=53)** | **Aseptic Loosening (n=12)** | **No Aseptic Loosening (n=41)** | **p-value** |
| **N** | **53** | **12** | **41** | |
| ***Periosteal-Stem Index (PSI)*** | | | | |
| Proportional annual rate; median (IQR) | 0.94 (-0.29–4.02) | 2.99 (1.15–6.57) | 0.3 (-0.48–3.41) | 0.054 |
| Log-time rate; median (IQR) | 0.1 (-0.01–0.25) | 0.24 (0.08–0.49) | 0.09 (-0.01–0.23) | 0.081 |
| ***Endosteal-Stem Index (ESI)*** | | | | |
| Proportional annual rate; median (IQR) | 1.76 (-0.29–9.27) | 9.27 (4.81–15.96) | 1.02 (-0.56–5.62) | 0.008* |
| Log-time rate; median (IQR) | 0.08 (-0.01–0.35) | 0.43 (0.24–0.64) | 0.05 (-0.02–0.18) | 0.003* |
| ***Cortical-Stem Index (CSI)*** | | | | |
| Proportional annual rate; median (IQR) | -1.22 (-8.5–2.58) | -4.58 (-8.55–4.2) | -1.16 (-8.5–2.11) | 0.903 |
| Log-time rate; median (IQR) | 0 (-0.12–0.09) | -0.11 (-0.31–0.07) | 0.01 (-0.08–0.11) | 0.179 |

All values: median (IQR). Mann-Whitney U test. For loosening patients, rates calculated TP1 → TP loosening. For non-loosening patients, rates calculated TP1 → TP2.