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Compressive Osseointegration Modular Prosthesis; Its Complications and Survival: A Systematic Review

Ryan Putra Wondany[1], Putu Astawa[1]

[1]Orthopaedic and Traumatology Department, Faculty of Medicine, Universitas Udayana/Prof. Dr. Ngoerah General Hospital, Denpasar, Indonesia

Corresponding Author: Ryan Putra Wondany

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ABSTRACT

Introduction: Minimal remaining bone is one condition that often complicates the limb salvage procedure. Compressive osseointegration is one of the latest modalities with a potential as a solution for this condition. While this modality is promising, the research on its effectivity and longevity on managing limb salvage in musculoskeletal tumor has not been widely studied, particularly in terms of complications and 5-year and 10-year implant survival rate.

Materials and Methods: We comprehensively searched PubMed, Google Scholar, Cochrane Library, Science Direct, and Scopus for researches related to compressive osseointegration up to May 2021, which resulted in 89 articles. All publications were then reviewed by the authors based on PRISMA guidelines, which qualified 10 articles for systematic review.

Results: Compressive osseointegration has been reported to have a high 5-year & 10-year survival rate, up to 95% and 93% respectively, which are comparable to earlier models of implants. Earlier studies reported mechanical failure and prosthetic infection to be the most common complications to occur in compressive osseointegration, and occurred mostly before their second postoperative year, where mechanical failure is mostly caused by fall and strenuous activities on younger patients.

Conclusion: Compressive osseointegration is a promising limb salvage endoprosthesis design. It offers capability of salvaging limb with minimal amount of bone remaining after resection. Complications that occur from using this endoprosthesis are mostly aseptic failure, which occurs within two years postoperatively, resulting in 5-year and 10-year survival rate of 85% and 81% respectively.

Keywords: compressive osseointegration, limb salvage, tumor, complication, survival

INTRODUCTION

One condition that often complicates the limb salvage procedure of musculoskeletal tumor is the minimal amount of remaining bone after resection. Compressive osseointegration modular prosthesis is one of the latest modality on endoprosthesis field which has a potential as a solution for this condition. This endoprosthesis utilizes compression mechanism exerted on the bone-prosthesis interface, thus promoting osseointegration and nullifying stress-shielding effect. While this modality is promising, the research on its effectivity and longevity on managing limb salvage in musculoskeletal tumor has not been widely studied, particularly in terms of complications and 5-year and 10-year implant survival rate.

Amputation was once the golden standard treatment for patients with massive musculoskeletal tumor. However, since the advent of chemotherapy, limb salvage has become a promising alternative.[1] Increasing the life expectancy of patients with musculoskeletal tumor, up to 80% in 5-

year survival rate, raises the concern of the long term solution for salvaging resected limbs.[2–4] Pioneered by Austin Moore in 1943, endoprosthetic replacement has become integral part in reconstructing the partially-resected limb.[1] Endoprosthesis has been proven to manifest excellent functional outcome towards amputation due to its ability in delivering solution with less infection risk.[5] Since then, various endoprosthesis has been developed to accommodate diverse types of massive bone loss due to musculoskeletal tumor, each of them are crafted to serve as a replacement for the resected bone and even the adjacent joint.[6] Materials and designs of endoprosthesis are constantly investigated to achieve an ideal implant, which exhibit these prominent properties: high corrosion and fatigue resistant, high biocompatibility and osseointegration potential, together with ultimate bone-implant stability.[7] However, these prostheses still aren't able to salvage limb with minimal amount of bone left after resection.

Compressive osseointegration endoprosthesis is one of the latest designs in endoprosthesis field. Having obtained FDA clearance for femur reconstruction, this device utilizes the nature of bone growth under compressive stress through the generation of 400 to 800 pound of force by titanium-coated spindle anchored to the bone through spring-loaded device via short traction bar on the bone-prosthesis interface.[2,8–10] This design not only enables surgeons to reconstruct short segment of remaining bone, up to 5 cm bone left, with satisfactory strength and stability, but also to seal the medullary canal, thus reducing the risk of osteolysis caused by debris infiltration.[11–14] It has been reported to reach 89% survival rate at 5 years and 80% at 10 years.[15,16]

Among the few studies reported its outcome, mechanical and biological failures of compressive osseointegration endoprosthesis have been reported.[2,8,9,13,15,17,18] The most consistent failure reported is related to spindle failure,[2,8,15,16,19] absence of bone-prosthesis interface osseointegration,[13,16,18,20–23] and periprosthetic fracture.[11,13,14,16,19,23]

This study aims to evaluate the current peer-reviewed literatures on the possible complications occurring on patients with compressive osseointegration endoprosthesis, identifying prognostic factors affecting the occurrence of the complications. Understanding these outcomes will be valuable for the clinicians and researchers.

MATERIALS & METHODS

Search strategy

A systematic review protocol was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[24,25] A comprehensive literature search was performed to identify all full-length, peer reviewed, English language studies on the mechanical and biological failures occurrence in musculoskeletal tumor patients managed compressive osseointegration, accompanied with their 5-year and 10-year survival rate until March 2021. Database searches were conducted on PubMed, Google Scholar, MEDLINE, Cochrane Library, Science Direct, and Scopus. The search term used was "Compressive osseointegration" AND "tumor".

Article selection

Article duplicates were removed, and remaining full-texts were reviewed and assessed against the inclusion/exclusion criteria independently by two authors. Additional articles were obtained by checking the references of the articles initially identified, and returned the articles found on the initial search. Inclusion criteria used on this study were: prospective or retrospective cohort study design, musculoskeletal tumor diagnosis with compressive osseointegration endoprosthesis limb salvage method, predictive factors for implant failures recorded. Exclusion criteria were case reports, reviews and critical reviews,

guidelines, and non-tumor patients. The review process is summarized on Fig. 1 diagram.

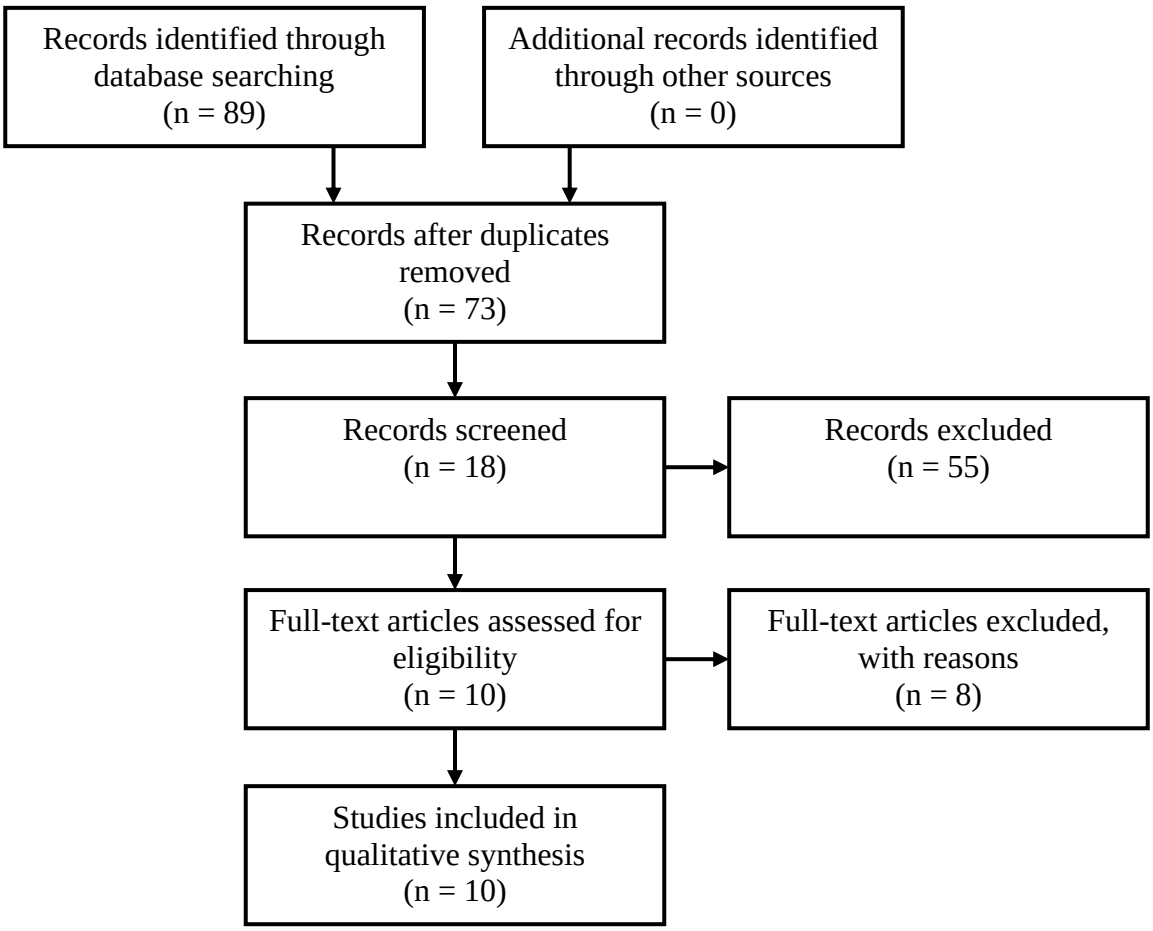

Fig 1. Systematic article search based on PRISMA guidelines.[24]

RESULT

A total of 89 articles were found from the searches. Sixteen articles were duplicates and removed. Filtering through inclusion and exclusion criteria further removed 63 articles. Through PRISMA guidelines, the filtering process resulted in 10 articles to be included in this systematic review. No additional relevant papers were found upon reviewing the references of the initial paper result. The study design and its patient's characteristics of each qualified paper are listed on Table 1 below, while the diagnosis, prosthesis location, resection length, and complications occurrence are listed on Table 2.

Table 1. Study design and patient characteristics of each study.

No.	Author	Journal Name	Study Design	LoE	Sample size	Mean age of patient (age range)
1	Avedian et al.	CORR	Prospective cohort	3	54 28M, 26F	19,5 years
2	Calvert et al.	CORR	Prospective cohort	3	50 25M, 25F	20,5 years
3	Goldman et al.	CORR	Retrospective cohort	3	79 49M, 30F	26 years (7-69 years)
4	Goulding et al.	CORR	Retrospective cohort	3	9 4M, 5F	45 years (21-62 years)
5	Healey et al.	CORR	Retrospective cohort	3	82 40M, 42F	20,4 years (14-63 years)
6	Kagan et al.	CORR	Prospective cohort	2	114 58M, 56F	N/R
7	Monument et al.	CORR	Retrospective cohort	3	18 9M, 9F	21 years (7-47 years)
8	O'donnell et al.	CORR	Retrospective cohort	3	16 7M, 9F	18 years (12-42 years)
9	Tyler et al.	CORR	Retrospective cohort	3	221	N/R
10	Zimel et al.	CORR	Retrospective cohort	3	27 14M, 13F	30 years (13-62 years)

LoE = level of evidence; CORR = Clinical Orthopaedics and Related Research M = Male; F = Female; N/R = not recorded

Table 2. Complication characteristics on each study.

No.	Author	Mean follow up duration	Diagnosis Primary/Revision	Anatomic location	Resection length (cm)	Complications occurred	Mean time to complication
1	Avedian et al.	16,6 months	Primary (44) Osteosarcoma (28) Posttraumatic deformity (7) Giant cell tumor (3) Ewing's sarcoma (2) Chondrosarcoma (2) Osteonecrosis (1) Fibrosarcoma (1) Revision (10)	Distal femur (54)	18.75-19.95	Cortical thickness growth retardation	N/R
2	Calvert et al.	68 months	Primary (50) Osteosarcoma (39) Chondrosarcoma (3) Ewing's sarcoma (3) Giant cell tumor (2) Malignant fibrous histiocytoma (1) Malignant pleomorphic meschencymal tumor (1) Desmoplastic fibroma (1)	Distal femur (37) Proximal femur (6) Proximal humerus (3) Proximal tibia (2) Intercalary femur (2)	17.8	Aseptic failure (9) Failed osseointegration (6) Component malrotation (1) Dislocation (2) Periprosthetic complications (6) Periprosthetic infection (6) Fracture distant to implant (1)	12,4 months (implant removal) 8,3 months (revision for aseptic failure)
3	Goldman et al.	84 months	Osteosarcoma (49) Chondrosarcoma (2) Ewing's sarcoma (5) Other malignant neoplasm (9) Aggressive benign neoplasm (14) Primary (54) Revision (25)	Distal femur (79)	13-36	Aseptic failure (28) Implant removal (11) Bone-spindle interface failure (8) Rotational failure (4) Traction bar failure (1) Aseptic loosening (1) Loss of spindle-anchor plug space (1) Taper adapter fracture (2) Periprosthetic complications (2) Periprosthetic fracture (1) Periprosthetic infection (1)	23 months (aseptic failure)
4	Goulding et	68 months	Revision (9)	Distal	N/R	Aseptic failure (5)	6 months (Periprosthetic

	al.		Osteosarcoma (2) Infection (3) Ewing's sarcoma (1) Other malignant neoplasm (2) Open fracture (1)	humerus (7) Proximal humerus (2)		Deficient bone support + lack of spindle fixation (1) Aseptic loosening (1) Polyethylene bushing exchange (1) Recurrent instability (2) Periprosthetic complications (3) Periprosthetic fracture (1) Prosthetic infection (2) Surgical complications (3) Nerve palsy (2; radial & ulnar) Skin infection (1)	fracture) 5 months (deficient bone support) 83 months (polyethylene bushing exchange)
5	Healey et al.	48,4 months	High-grade osteogenic sarcoma (64) Chondrosarcoma (5) Malignant fibrohistiocytoma (5) Giant cell tumor (3) Low-grade osteogenic sarcoma (2) Other tumor (1) Revision arthroplasty (2) Primary (64) Revision (18)	Distal femur (82)	N/R	Aseptic failure (13) Aseptic loosening (3) Failed osseointegration (5) Absence of bone growth (5) Periprosthetic complications (15) Periprosthetic fracture (10) Periprosthetic infection (5) Local recurrence (3)	2 years (2) > 2 years (5) > 5 years (1)
6	Kagan et al.	4 years	Primary (40) Revision (74)	Distal femur (64) Proximal femur (37) Proximal tibia (13)	N/R	Aseptic failure (7) Mechanical failure (6) Dysvascular leg (1) Periprosthetic complications (19) Periprosthetic fractures (2) Periprosthetic infection (17) Local recurrence (1)	N/R
7	Monument et al.	8 years	Primary (12) Osteosarcoma (8) Malignant fibrous histiocytoma (1) Ewing's sarcoma (2)	Distal femur (15) Proximal femur (3)	17-19	Aseptic failure (8) Component removal (6) Mechanical failure (2) Periprosthetic complications (3)	21 months (all complications) All failures occur before 30 months

			Undifferentiated pleomorphic sarcoma (1) Revision (6) Osteosarcoma (5) Chondrosarcoma (1)			Periprosthetic infection (2) Arthrofibrosis (1) Local recurrence (1)	
8	O'donnell et al.	4,5 years	Primary (16) Osteosarcoma (12) Ewing's sarcoma (2) Chondrosarcoma (1) Undifferentiated sarcoma (1)	Proximal tibia (16)	17	Aseptic failure (2) Aseptic loosening (1) Failed osseointegration (1) Periprosthetic complications (3) Periprosthetic infection (3)	4,5 years to first failure report
9	Tyler et al.	58 months (periprosthetic fracture) 37,75 months (non-periprosthetic fracture)	Primary (170) Revision (51)	Distal femur (154) Proximal tibia (38) Proximal femur (23) Distal humerus (4) Proximal humerus (2)	N/R	Periprosthetic complications (6) Periprosthetic fracture (6)	N/R
10	Zimel et al.	96,25 months	Revision (27) High-grade osteogenic sarcoma (20) Parosteal osteogenic sarcoma (2) Chondrosarcoma (1) Malignant fibrous histiocytoma (1) Another tumor (2) Infected periprosthetic fracture (1)	Distal femur (27)	N/R	Aseptic failure (3) Mechanical failure (3) Periprosthetic complications (4) Periprosthetic infection (4)	39 months to prosthetic infection 6,25 months to mechanical failures
			N/R = not recorded				

DISCUSSION

Compressive osseointegration is a breakthrough in the field of limb salvage surgery for patients with musculoskeletal tumor. Its design requires only at least 5cm of remaining bone for installation, and is able to prevent stress shielding that complicates earlier endoprosthesis models.[11,26] The compression exerted on the bone-prosthesis interface stimulates bone deposition, thus reinforcing the osseointegration process.[13,19]

However, just as its predecessor, compressive osseointegration usage has its own complications. This review has discovered that the most common complication is classified under aseptic failure, which consists of failed osseointegration, aseptic loosening, and mechanical failure.[2,9,11] These complications, which mostly occur in the first two years of postoperative period, will require patients to undergo revision surgery, which can be a implant removal or implant revision surgery.[2,11,15,19] Periprosthetic complications such as periprosthetic fractures and infection is the second most commonly occurred complication.[9,11,15,19,27] Several authors have found that mechanical failure mostly occur earlier in the postoperative period than periprosthetic complications.[9,11,27] The 5-year survival rate of this endoprosthesis ranges from 67% to 85% for overall failure.[2,15–17,27] By excluding the infection complications, the survival rate increases up to 95%, indicating that the periprosthetic infection greatly affects the prosthesis survival rate.[2,17] The studies used in this review have shown this endoprosthesis 10-year survival rate ranges from 71% to 81%, that increases up to 93% by excluding periprosthetic infection complications.[2,16,17,27]

Several correlations have been found by the papers included in this review. Avedian et al. has concluded that chemotherapy can result in decreased osseointegration process measured through decreased cortical thickness growth around the bone-prosthesis interface compared with patients not receiving chemotherapy, while Kagan et al. found correlation between radiotherapy with increased prosthesis failure rate.[17,20] Calvert et al. and Goldman et al. have concluded that the rate of complication occurrence is not correlated with prosthesis-related variables, rather, the patient's activity is, especially rotational movements.[2,9] The distal femur endoprosthesis has been correlated with higher incidence of rotational failure as reported by Goldman et al., with the retention rate of 91%, while Kagan et al. reported decreased risk of failure on cases of endoprosthesis reconstruction on proximal femur.[2,17] A research by Monument et al. have observed the incidence of mechanical failure of this endoprosthesis used in pediatric patients increases due to ground-level fall, and all of them occurred within 30 months after salvage procedure.[15] Research by Zimel et al. has concluded that non-compliance to non-weight bearing restriction has resulted in increased mechanical failure rate, which often occurs in young patients within 6,25 months postoperatively.[27]

CONCLUSION

Compressive osseointegration is a promising limb salvage endoprosthesis design. It offers capability of salvaging limb with minimal amount of bone remaining after resection. Complications that occur after limb salvage surgery using this endoprosthesis are mostly aseptic failure, which occurs within two years postoperatively, that resulted in 5-year and 10-year survival rate up to 85% and 81% respectively. Strict adherence to non-weightbearing restriction and careful movements can reduce the complication occurrence.

Declaration by Authors

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