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Original Article

Comparative Analysis and Evaluation of Functional Outcome of Extended Curettage, Cauterization of Margins with Appropriate Fixation, and Bone Cementing with or without Incorporation of Zoledronic Acid Powder in Grade III Campanacci Giant Cell Tumor Around Knee Joint

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Abstract

Introduction: Treatment of giant cell tumors (GCT) Campanacci grade III remains challenging till date because of the high recurrence rate of the disease and notorious post-operative complications which lead to significant morbidity in patients. Among the various types of surgical procedures, we chose extended curettage, cauterization of margins followed by appropriate fixation, and bone cementing with and without incorporation of zoledronic acid. This study was conducted to evaluate the functional outcome of the aforementioned procedure.

Materials and Methods: A prospective analytical study of 10 patients of grade III Campanacci GCT was included in the study and all patients were planned for surgical intervention and included in this study. The patients were randomly divided into two groups, of which one group was taken for extended curettage, cauterization of margins followed by appropriate fixation with bone cementing alone, and in the other group same procedure was done with the incorporation of zoledronic acid in bone cement. Lysholm scoring was used to evaluate the outcome in follow-up.

Results: The mean Lysholm score in the pre-operative period was 0.5, whereas the mean Lysholm score at 6 weeks was 21.5, 74.7 at 12 weeks, and 87.5 at 24 weeks post-operative period. Upon comparison between the mean Lysholm score at 6, 12, and 24 weeks post-operative period in the zoledronic acid application group and zoledronic acid non-application group, it was 21.80 versus 21.20 (P = 0.412), 75 versus 74.40 (P = 0.644), and 89 versus 86 (P = 0.111), respectively. Regarding post-operative complications among the study subjects, a total of 3 patients (30%) developed post-operative complications, among which 2 patients developed swelling (20%) and 1 patient (10%) developed joint pain.

Conclusion: Although not statistically significant, there was a trend of better functional outcomes in terms of the Lysholm scoring system in cases of grade III Campanacci GCT around the knee joint treated with extended curettage, cauterization of margins with appropriate fixation, and bone cementing with or without incorporation of zoledronic acid powder.

AQ1 **Key words:** Campanacci grade III giant cell tumor, Zoledronic acid

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INTRODUCTION

Bone tumors comprise <1% of all neoplasms. Giant cell tumor comprises 5–10% of all primary bone tumors.[1] Although, giant cell tumor of bone is generally considered a benign tumor commonly seen around the knee joint mostly in young and middle-aged populations. It is well

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known for its locally aggressive behavior and its potential for recurrence and occasionally pulmonary metastasis.

A giant cell tumor is a lesion that continues to fascinate orthopedic surgeons with its behavior, appearance, and the various treatment options available. Around 1–3% of giant cell tumors (GCT) are primarily malignant or have the potential to undergo malignant transformation and metastasis.[2]

As per the treatment selection, there is no specific method described for the same. There are various surgical techniques from intra-lesional curettage to wide resection and reconstruction. The goals of treatment are the elimination of the tumor, preservation of the limb, and prevention of local recurrence and distant metastasis. Many authors have advocated *en-bloc* resection and megaprosthesis as good treatment options in grade III Campanacci tumors as it has less local recurrence rates, but if any patient requires revision surgery, then there are less joint functional preservation surgery options available. However, the procedure done in the current study, i.e., extended curettage, cauterization of margins with appropriate fixation, and bone cementing alone, and those treated by extended curettage, cauterization of margins with appropriate fixation, and bone cementing with zoledronic acid powder incorporated in the cement is also good treatment option in grade III Campanacci tumor around the knee joint as it provides an option for revision surgery if required, especially in a young patient with better joint function and preservation. During the last decade, several adjuvant methods have been advocated apart from simple curettage to facilitate better local control and prevent recurrences. In our current study, the aforementioned procedure and surgical technique are more cost-effective and also have joint function preserving.

MATERIALS AND METHODS

This was a prospective analytical study in which all the patients diagnosed with Campanacci grade III extra compartmental GCT around the knee joint admitted under the Department of Orthopaedics, Dr. BRAMH, Raipur (C.G.) from January 2022 to August 2022, meeting the inclusion criteria were included.

Patients were allocated into two different groups randomly by the 1-2 1-2 method, one in which patients were subjected to extended curettage, cauterization of margins with appropriate fixation, and bone cementing alone, and in the other group extended curettage, cauterization of margins with appropriate fixation, and bone cementing with zoledronic acid incorporation was done.

Assessment of the knee score was done using Lysholm knee score, both pre- and postoperatively in each follow-up. As the score involved weight-bearing activities, the score calculation was done at 6-, 12-, and 24-week postoperatively.

After obtaining the Tegner-Lysholm knee score for both groups the comparison between both groups was done and tests of significance were applied.

A total of 10 subjects including seven women and three men of age ranging from 18 to 45 years (mean 26.1 years) were selected for operative intervention after they were provisionally diagnosed clinically, radiologically (X-Ray), and histopathologically (FNAC, Biopsy) with GCT around the knee joint.

Campanacci *et al.*[3] a grading system was used to select GRADE III GCT around the knee joint. AQ2

Functional outcomes were evaluated using the Lysholm scoring system[4] at serial intervals of 6, 12, and 24 weeks post-operative.

Inclusion Criteria

The following criteria were included in the study:

- Confirmed (radiological and pathological) cases of extra compartmental GCT
- GCT around the knee joint that is the proximal tibia and distal femur
- Patient giving consent for extended curettage with bone cementing therapy between 2021 and 2022
- Campanacci grade III GCT.

Exclusion Criteria

The following criteria were excluded from the study:

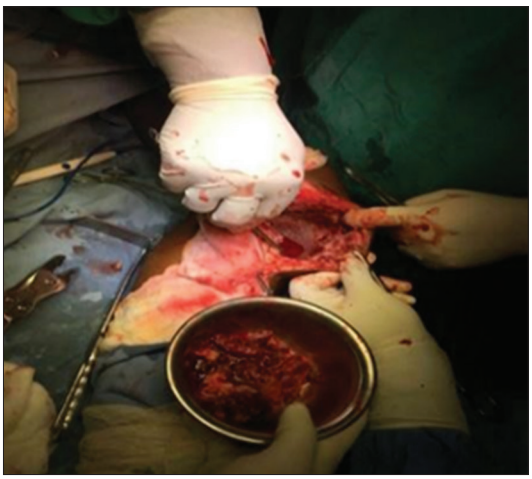
- GCT with metastasis and/or multi-organ involvement
- Immuno-compromised patients
- Pre-existing joint disease
- Intra compartmental GCT (Grade I/II Campanacci)
- GCT involving neurovascular structures.

Surgical Procedure

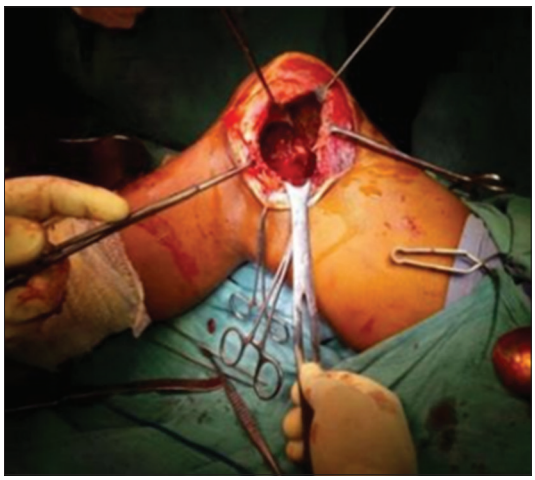
First of all, the tumor was exposed from the side of maximum cortical destruction such that all the biopsy tracts could be excised with the same incision. Then, thorough removal of the tumor tissue was done with continuous irrigation, suction, and curettage that led to the formation of a large cavity, the margins of the cavity were now thoroughly coagulated with a cautery.

Then the cavity was packed with hydrogen peroxide for some time to cause thermal cautery of the remaining tumor tissues. Since the tumor is extra-compartmental the eroded bone is supported by a buttress plate. After

AQ5 **Figure 1: Tumor is exposed from the side of maximum cortical destruction**



AQ5 **Figure 2: Thorough removal of tumor tissue is done with continuous irrigation, suction, and curettage**



AQ5 **Figure 3: Formation of the large cavity after curettage**

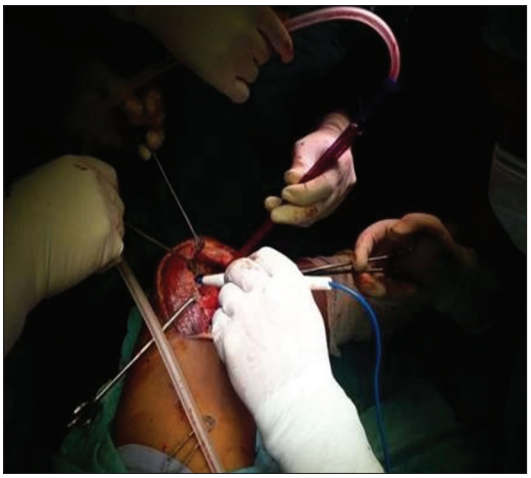


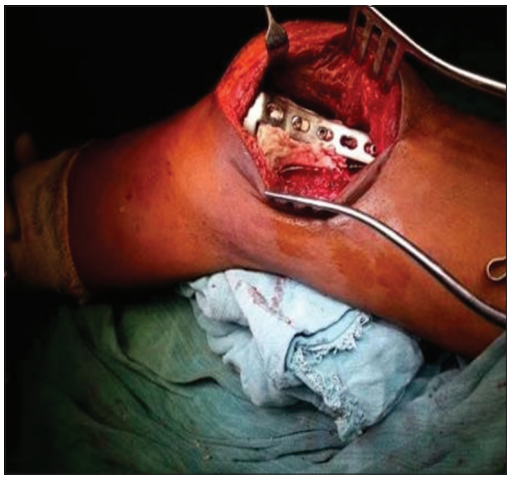
Figure 4: Margins are thoroughly coagulated with cautery AQ5

Figure 5: Eroded bone is given support by a buttress plate AQ5

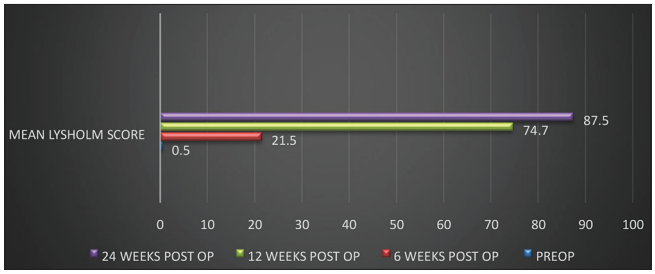
Figure 6: Cavity is filled with bone graft on the subchondral surface AQ5

plate positioning the cavity is filled with bone graft, or it can be done in the order that first graft incorporation followed by plating, then abgel is placed between the bone graft cement interface and especially over the graft placed subchondral near the articular surface. Finally, the residual cavity is packed with cement and the plate is held further with the screws.

AQ5 **Figure 7:** **Abgel is placed between the bone graft and cement interface**



AQ5 **Figure 8:** **Finally, the residual cavity is packed with cement and the plate is held further with screws**



AQ5 **Figure 9:** **Mean Lysholm score: Pre-operative, 6 weeks post-operative, 12 weeks post-operative and 24 weeks post-operative**

RESULTS

The mean age of the study subjects was 26.1 years, whereas the mean age among the study subjects in whom zoledronic acid incorporation was done was 25.40 years, and among those in whom zoledronic acid incorporation was not done was 26.80 years.

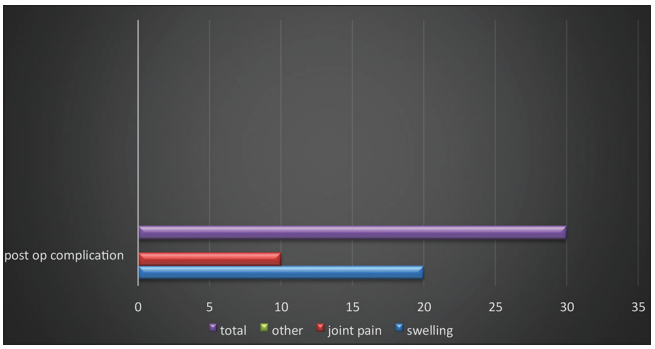


Figure 10: **Post-operative complications among the study subjects** AQ5

Out of 10 patients, there were 3 male patients (30%) and 7 female patients (70%).

The most common site of the tumor was the distal femur ($n = 7$), followed by the proximal tibia ($n = 3$).

The mean Lysholm score in the pre-operative period was 0.5, whereas the mean Lysholm score at 6 weeks was 21.5, 74.7 at 12 weeks, and 87.5 at 24 weeks in the post-operative period.

Upon comparison between the mean Lysholm score at 6, 12, and 24 weeks post-operative period in the zoledronic acid application group and the zoledronic acid non-application group, it was 21.80 versus 21.20 ($P = 0.142$), 75 versus 74.40 ($P = 0.644$), and 89 versus 86 ($P = 0.111$), respectively.

Regarding post-operative complications among the study subjects, a total of 3 patients (30%) developed post-operative complications, among which 2 patients developed swelling (20%) and 1 patient (10%) developed joint pain.

Table 1 shows the status of the overall mean Lysholm score in the pre-operative period and the mean Lysholm score at 6, 12, and 24 weeks post-operative period. The mean Lysholm score in pre-operative period was 0.5, whereas the mean Lysholm score at 6 weeks was 21.5, 74.7 at 12 weeks post-operative period, and 87.5 at 24 weeks post-operative period among the study subjects.

Table 2 shows the data regarding post-operative complications among the study subjects. A total of 3 patients (30%) developed post-operative complications, among which 2 patients developed swelling (20%) and 1 patient (10%) developed joint pain. Recurrences were not seen in any groups.

DISCUSSION

GCT is considered to be a benign lesion, despite its potential for local aggression, recurrence, and occasional

Table 1: Lysholm score pre-operative and post-operative period

S. No	Pre-operative Lysholm score	Post-operative Lysholm score 1.5 months	Post-operative Lysholm score 03 months	Post-operative Lysholm score 06 months
1	0	22	76	90
2	0	23	74	91
3	0	22	78	90
4	5	22	75	90
5	0	20	72	84
6	0	22	74	86
7	0	22	76	90
8	0	20	72	86
9	0	20	76	84
10	0	22	74	84
Mean	0.5	21.5	74.7	87.5

Table 2: Post-operative complications among study subjects

S. No	Post-operative complications	Frequency	Percentage
1.	Swelling	02	20
2.	Joint pain	01	10
Total		03	30

lung metastases. The frequency of these is approximately 1–3%, which can be higher in cases with local recurrence, especially when located in the soft tissue.[5]

This tumor does not remain latent. A small lesion tends to evolve and lead to the progressive destruction of the affected bone.[6] Therefore, surgical treatment should be indicated and performed as early as possible.

Most of the cases of GCT are preferentially treated with curettage associated with an adjuvant method.[7] This option leads to a better functional outcome but is associated with a higher chance of relapse, as evidenced in some of the studies.[8,9] As in wide resection the tumor is entirely removed, and it has the advantage of a lower chance of relapse. It is usually reserved for cases of extensive bone destruction, in which joint reconstruction is not feasible.[7,10] Various studies have advocated the use of this technique in Campanacci III tumors, aiming to reduce the risk of recurrence and biomechanical failure.[8,11] In some cases, without marked functional impairment, such as in the ulna, fibula, and small bones of the hand and foot, complete bone resection can also be performed.[6,7,12]

Since patients affected by this type of tumor are usually young, and therefore there is a concern to preserve the joint surface and to avoid possible early arthroplasty. Joint replacement by non-conventional endoprosthesis comes with some disadvantages, such as the need for revision and the risk of successive revisions. Thus, some studies indicate a preference for more conservative reconstruction methods in the treatment of these lesions, in the hope that the primary procedure will be definitive. The use of bone cement is a well-established method that presents good long-term oncological and functional results.

In the present study, we did extend curettage, and cauterization of the margin with appropriate fixation and bone cementing in five patients, and a similar procedure with the incorporation of zoledronic acid in another five patients. Functional outcome was assessed with Lysholm score at 6 weeks, 12 weeks, and 24 weeks in both groups. The mean Lysholm score at 6 weeks in zoledronic acid application group was 21.80 as compared to 21.20 in non-zoledronic acid application group.

The mean Lysholm score at 12 weeks in the zoledronic acid application group was 75 as compared to 74.40 in the non-zoledronic acid application group. The mean Lysholm score at 24 weeks in zoledronic acid application group was 89 as compared to 86 in non-zoledronic acid application group.

Singaravadivelu and Kavinkumar did a similar study and reported that at 3 months, the mean Lysholm score in zoledronic acid application group was 67 as compared to 56 in non-zoledronic acid application group.[13]

Yu *et al.* (2012) reported that at 24 weeks the mean Lysholm score[14] in zoledronic acid application group was 79 as compared to 68 in non-zoledronic acid application group.[15] AQ2

The procedure done in the present study is a good treatment option for the grade III Campanacci tumors around the knee joint. However, there was no statistically significant improvement in those who extended curettage, cauterization of margins with appropriate fixation, and bone cementing with zoledronic acid application compared to non-zoledronic acid application group in the present study.

There is a variation in the GCT recurrence incidence rates in the literature. Dahlin *et al.*[16] published a study with 60%

local recurrence in GCT patients who underwent curettage and grafting and recommended a more aggressive resection for local control. The use of methyl methacrylate associated with cauterization of the cavity as local adjuvants in the treatment of GCT significantly decreased the rate of recurrence.[11] In a literature review, Zhen *et al.*[9] showed varying recurrence rates, from 12% to 54% within 7 years of follow-up. Klenke *et al.*[10] observed recurrence rates ranging from 0% to 65%, depending on surgical method.

In the present study, we did not observe any recurrence in the first 24 weeks of post-operative period. However, unlike other studies, only locally aggressive Campanacci III tumors were included in the present study.

Various authors in their study have mentioned the local recurrence rates as: 13.6%% in 48 months follow-up,[17] 13.6% in 24–48 months,[18] 44% in 24 months,[19] 25.3% in more than 6 months,[15] 73.6% in 3–28 months,[13] 27% in 1–240 months,[20] 15% in 24–40 months,[12] and 23.3% in 59 months.[8]

There are different post-procedure complications that were reported among various studies such as infection, loosening of cement, loosening of prosthesis or implant, and graft failure.

Xiuchun *et al.*[4] in their study reported 10.5 % infection, 15.7% prosthesis aseptic loosening, and 5.26% peri-prosthesis fracture. Natarajan *et al.*[21] their study reported 6.9% infection, 8.3%% peri-prosthetic fracture, and 4.2% aseptic loosening. Ayerz *et al.*[17] in their study reported one patient had a subchondral collapse. Rigollino *et al.*[22] in their study reported two cases of pathological fractures. Zhang *et al.*[23] in their study reported five cases of infection and four cases of graft rejection. Vult Von Steyern *et al.*[24] in their study reported four cases of pathological fractures. AQ2 Mcgough *et al.*[20] in their study reported three cases of arthritis. Asavamongkolkul *et al.*[20] in their study reported no complications.

In our study, only three participants developed complications in which swelling was present in two of the study subjects whereas one patient developed pain around the knee joint which was associated with extraneous activity.

We cannot comment on post-operative complications based on our study because of the short duration of follow-up.

Baptista *et al.*[25] indicated that in the presence of fractures with significant deviation, marked deformity, or significant impairment of three cortical areas, the safest procedure is segment resection, from both the oncological standpoint and to reduce morbidity. The author concluded that the approximate volume of the tumor, presence of cortical involvement, percentage of the epiphysis width affected, and distance between the lesion border and the articular surface were statistically significant radiographic parameters for the indication and/or prognosis of the treatment with curettage associated with electrocauterization of the lesion wall and filling with bone graft, a technique assessed in his study. The prognosis of the tumor is directly related to the quality of the curettage technique and/or resection used, and not only to the method of reconstruction or filling.[6,8,11]

The presence of tumor extension to soft tissues and pathological fracture is a controversial subject in the literature.[7] McDonald *et al.*[26] in their study concluded that the possibility of tumor recurrence does not increase with pathological fracture. However, the association was not statistically significant. O'Donnell *et al.*[27] reported that three out of six patients (50%) with pathologic fractures evolved with recurrence of the tumor. They concluded that there is a correlation between the occurrence of pathological fractures and tumor recurrence. Jesus-Garcia *et al.*[8] indicated that pathological fracture may be an important factor in the association with recurrence, since in its presence, the difficulty in performing effective curettage is greater. In their study, of the eight patients who presented recurrence, 50% had a pathological fracture.

In the present study, comment on whether the chance of tumor recurrence was directly related to the presence of pathological fracture was not possible. However, the authors believe that the contamination of the soft tissue by the tumor, and pathologic fracture, is a risk factor for tumor recurrence.[8]

The present study is conducted with the purpose of studying and observing the functional outcome of treatment of Campanacci grade III GCT with extended curettage, cauterization of margins with appropriate fixation, and bone cementing, thereby preserving the joint structure and function at the Department of Orthopaedics at Pt. JNM Medical College and associated Dr BRAM Hospital, Raipur (C.G.).

In the present study, the mean age in zoledronic acid application group was 25.40 years as compared to 28.40 in non-zoledronic acid application group.

Age-wise distribution among the zoledronic acid application group shows that 40% each were between 18 and 25 years and 26–30 years' age group. Whereas in non-zoledronic acid application group shows that 40% each were between 18–25 years and 26–30 years' age group.

In the present study, gender-wise distribution among zoledronic acid application group shows that 80% were female, and non-zoledronic acid application group 60% were female.

Rigollino *et al.* (2017) in a similar study reported that a predominance of males was observed. Out of nine patients evaluated, seven were male (77.7%) and two female (22.2%). Patient age ranged from 26 to 41 years.[22]

Singh *et al.* also reported that the patient population's mean (SD) age was 24.04 (4.73) years with an age range of 18–34 years. Out of these 25 patients, there were 14 females and[28] 11 males.

In the present study site of GCT among zoledronic acid application group shows that 40% had a right distal femur and 40% had left distal femur and non-zoledronic acid application group 40% had left distal femur and 40% had left proximal tibia.

Kundu *et al.*[29] reported that the various sites of GCT were femur ($n = 16$), tibia ($n = 13$), radius ($n = 7$), and olecranon ($n = 1$). The mean volume of GCT was 31.29 cm^3 and 32.20 cm^3 in the study and control groups, respectively.

Rigollino *et al.* (2017) in a similar study reported that 70% had distal femur and 30% had left proximal tibia.[22]

Singh *et al.* also reported that out of the 14 patients who had involvement in the distal femur, there were eight females and six males. The 11 patients with involvement of proximal tibia included six females and five males.[28]

Asavamongkolkul *et al.* reported that out of the 54 patients, the anatomical site of the lesions included 35 distal femurs and 19 proximal tibias.[20]

In the present study, the mean Lysholm score at 6 weeks in zoledronic acid application group was 21.80 as compared to 21.20 in non-zoledronic acid application group.

In the present study, the mean Lysholm score at 12 weeks in zoledronic acid application group was 75 as compared to 74.40 in non-zoledronic acid application group.

In the present study, the mean Lysholm score at 24 weeks in zoledronic acid application group was 89 as compared to 86 in non-zoledronic acid application group.

Singaravadivelu and Kavinkumar did a similar study and reported that at 12 weeks the mean Lysholm score in the zoledronic acid application group was 67 compared to 56 in non-zoledronic acid application group.[13]

Yu *et al.* (2012) reported that at 24 weeks the mean Lysholm score in zoledronic acid application group was 79 as compared to 68 in non-zoledronic acid application group.[15]

Kumar *et al.* study the role of Zoledronic Acid Supplementation in Reducing Post-Surgical Recurrence of Giant Cell Tumor of Bone. They reported that the zoledronic acid supplementation was associated with significantly lower tumor recurrence rates ($P = 0.007$). In addition, a significant association of soft-tissue extension and non-usage of PMMA cement with tumor recurrence was observed.[30]

CONCLUSION

This study concludes that there is definitely an improvement in the functional outcome in terms of Lysholm score in grade III Campanacci GCT around knee joint treated with extended curettage and cauterization of margins with appropriate fixation and bone cementing with or without incorporation of zoledronic acid.

Furthermore, this procedure is economical and there is better patient compliance noted when compared to other Campanacci grade III GCT around knee joint interventions such as en block resection and megaprosthesis.

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