



# The impact of metabolic syndrome on clinical outcomes following total knee arthroplasty in osteoarthritis patients

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**Background:** Metabolic syndrome (MetS) is a combination of interconnected conditions, including insulin resistance, abdominal obesity, high blood pressure, and abnormal blood lipid levels. The objective of this research was to investigate the impact of MetS on the quality of life and clinical outcomes following total knee arthroplasty (TKA) in patients with osteoarthritis (OA).

**Methods:** A retrospective descriptive study was conducted to enroll OA patients who underwent primary TKA at Zhongda Hospital, Southeast University from January 2015 to August 2019. A total of 83 OA patients who did and 144 (MetS group) who did not have MetS (non-MetS group) were included. An analysis was conducted on the patient's clinical data.

**Results:** The two groups had similar results in terms of lengths of stay ( $P=0.93$ ), hospital costs ( $P=0.24$ ), and overall complication rates ( $P=0.99$ ). There was no significant difference in the average erythrocyte sedimentation rate and C-reactive protein levels between the groups. However, the MetS group exhibited notably lower Hospital for Special Surgery knee scores and Short Form [36] health survey (SF-36) scores compared to the non-MetS group (both  $P>0.05$ ) during the one-year follow-up period.

**Conclusions:** OA patients who have MetS had significantly worse knee joint function and quality of life after TKA. There are certain constraints in the current research. First, it belongs to a single-center retrospective study. Further study will be necessary to determine the generality of this conclusion. Second, this study is retrospective, and the number of patients included is not large. Third, due to the diverse clinical groups in our hospital, it is challenging to comprehensively document all the clinical data of the patients involved in this study. Forth, this study did not compare the preoperative differences between the two groups, as well as analyze the postoperative improvement changes in depth. We will compare the preoperative and postoperative differences between the two groups in more depth in future large sample studies.

**Keywords:** Metabolic syndrome (MetS); osteoarthritis (OA); total knee arthroplasty (TKA); Hospital for Special Surgery knee scores; Short Form [36] health survey (SF-36)

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## Introduction

Osteoarthritis (OA) is a prevalent joint disease, affecting approximately 250 million individuals globally (1). Significant investments have been made in research and treatment for OA. Among adults aged 65 and above, OA of the knee affects 60% of adults (2). The pathogenesis of OA is multifaceted, with the disease closely related to inflammatory factors and metabolism (3). Investigations exploring comorbidity in OA have revealed the coexistence of chronic conditions, including hypertension, cardiovascular diseases, obesity, and diabetes (4).

Metabolic syndrome (MetS), also known as insulin resistance syndrome, is a complex metabolic disorder (5). MetS encompasses a range of conditions, including insulin resistance, hypertension, increased plasma triglycerides, decreased high-density lipoprotein cholesterol, obesity, and proteinuria (6). OA, a degenerative joint disease, is impacted by various structural and metabolic elements (7). Metabolic OA, a phenotype of OA, is closely associated with MetS and obesity (8). Metabolic OA mainly affects people between the ages of 45 and 65 years who have widespread OA, are overweight or obese, and exhibit at least one component of MetS, such as diabetes, high blood pressure, or abnormal lipid levels (9). Numerous studies have provided support for the concept of metabolic OA, demonstrating a higher prevalence of OA in patients with MetS (10,11). Notably, MetS was detected in 59% of the OA population, whereas only 23% of the non-OA group had MetS (6). Furthermore, emerging evidence suggests that individuals with MetS are more prone to developing OA. The initiation of the OA process involves

factors such as adipokines, insulin resistance, systemic inflammation of low intensity, and lipid toxicity.

Metabolic disorders exhibit intricate interactions with OA through diverse mechanisms, including the induction of chronic low-grade systemic inflammation and the release of adipokines such as adiponectin (12), leptin (13), IL-6 (14), lipocalin-2 (15), and other related secretory phenotypic factors implicated in chondrocyte senescence. These interactions not only modulate systemic and local joint-related autoimmune and inflammatory processes but also facilitate macrophage polarization and enhance apoptosis of articular chondrocytes (16,17). Due to the significant role of metabolic diseases in OA development, there is an increasing focus on the emerging subtype of metabolic OA. Nevertheless, the effect of MetS on the prognosis of OA patients remains inconclusive in clinical studies.

The association between OA and MetS has been previously established across diverse cultural contexts (18,19). However, the role of MetS in OA pathogenesis has been little studied. In this study, the clinical data of patients undergoing total knee arthroplasty (TKA) for knee OA were collected to explore the effect of OA patients with MetS on knee function and quality of life after TKA, to reveal the effect of MetS on the complete course of OA, and to strengthen the attention to the early diagnosis and treatment of OA patients. We present this article in accordance with the STROBE reporting checklist (available at <https://aoj.amegroups.com/article/view/10.21037/aoj-24-2/rc>).

## Methods

### Populations

A total of 609 patients who received TKA at Zhongda Hospital, Southeast University between January 1, 2015, and August 31, 2019, were enrolled in this retrospective study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Clinical Research Ethics Committee of Zhongda Hospital, Affiliated to Southeast University (IRB No. 2020ZDSYLL206-P01) and individual consent for this retrospective analysis was waived. *Figure 1* illustrates the study design flowchart. Eligible patients (n=227) must meet all of the following inclusion criteria: (I) both MetS and end-stage knee OA should align with their respective diagnostic criteria; (II) patients had received TKA for the first time; (III) the patients and their families should have

### Highlight box

#### Key findings

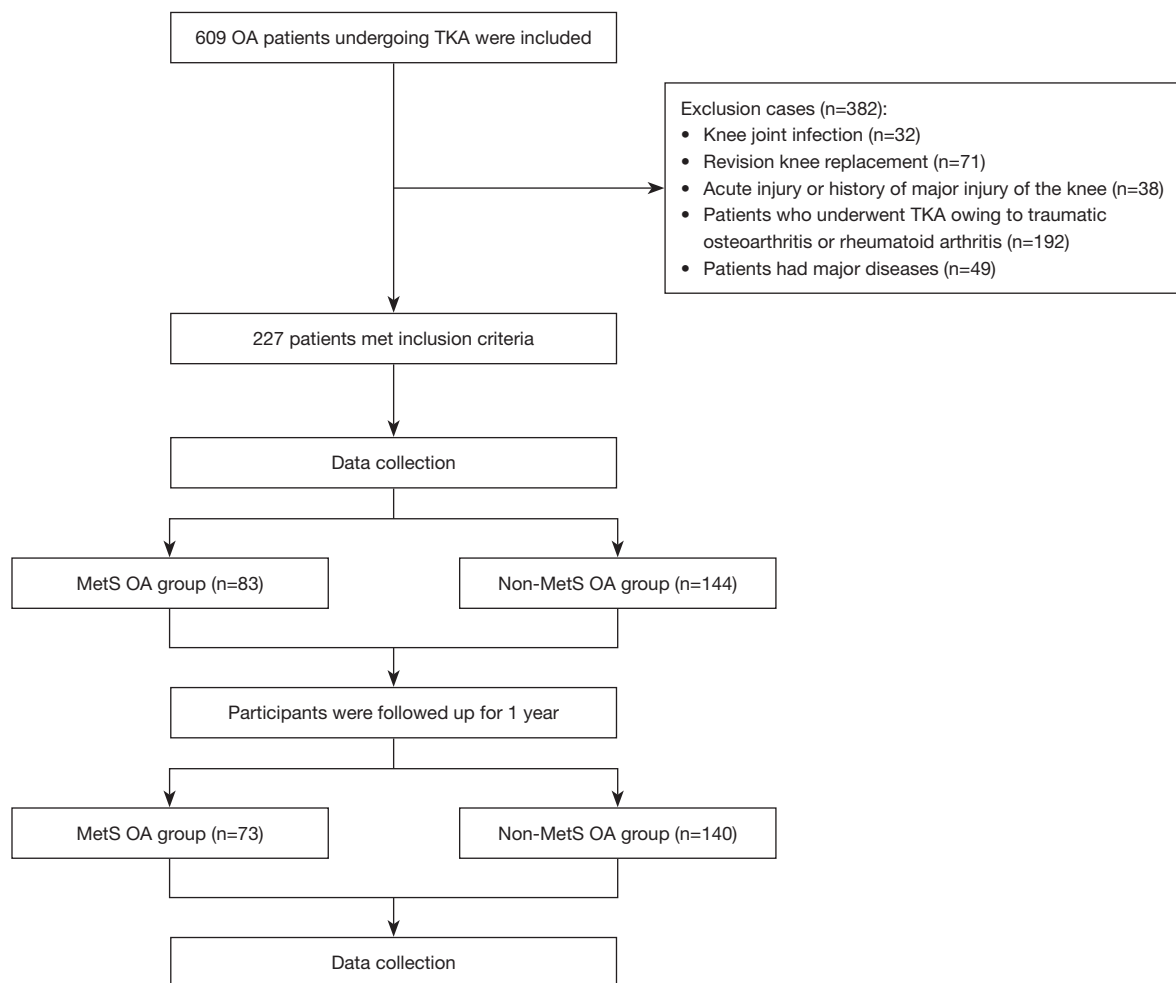
- A significant decline in knee joint function and quality of life was observed after total knee arthroplasty (TKA) for patients with osteoarthritis (OA) who have metabolic syndrome (MetS).

#### What is known and what is new?

- Emerging evidence supports that people with MetS are more susceptible to develop OA.
- OA patients with MetS will also affect the clinical outcome after TKA.

#### What is the implication, and what should change now?

- MetS should be assessed before TKA in OA patients.
- Early diagnosis and treatment of MetS, especially in the elderly can prevent many adverse impact of MetS.



**Figure 1** Study flow chart. Mets, metabolic syndrome; OA, osteoarthritis; TKA, total knee arthroplasty.

signed the informed consent for the surgical procedure; and (IV) complete clinical data and follow-up data should be available. The exclusion criteria are as follows: (I) knee joint infection or revision knee replacement; (II) acute injury or history of major injury of the knee; (III) patients who underwent TKA owing to traumatic OA or rheumatoid arthritis; (IV) patients had major diseases, such as heart disease, infectious diseases, mental illness, cognitive dysfunction, and secondary knee joint OA.

At least thirty of the surgical cases were performed by four adult reconstruction surgeons who have received fellowship training. A standard medial parapatellar approach was consistently employed in all cases, with appropriately sized prostheses being installed into the tibia and femur. Cemented implants were utilized for all included patients, and intravenous antibiotics were administered for 24 h

following the surgery.

### **Grouping method**

Patients diagnosed with MetS were identified based on the criteria outlined in the Guidelines for the Prevention and Treatment of Type 2 Diabetes in China (20). These criteria included the presence of at least 3 of the following abnormalities: (I) central obesity (waist circumference  $\geq 90$  cm for males and  $\geq 85$  cm for females); (II) hyperglycemia (fasting plasma glucose  $\geq 6.1$  mmol/L or 2 h postprandial glucose  $\geq 7.8$  mmol/L); (III) elevated blood pressure ( $\geq 130/85$  mmHg or current hypertension treatment); (IV) high levels of triglycerides ( $\geq 1.70$  mmol/L); and (V) low HDL cholesterol ( $< 1.04$  mmol/L). According to the Kellgren and Lawrence classification (21), every patient

exhibited severe OA of the knee, graded as III or IV. The patients with OA were divided into two groups depending on whether they were diagnosed with MetS (MetS, n=73) or not diagnosed with MetS (non-MetS, n=140).

### Data collection

According to the information from the orthopedic surgery database of Zhongda Hospital, Affiliated to Southeast University, the electronic medical records of TKA patients were exported from the HIS system. The clinical data of the patients who fulfilled the criteria were chosen based on the inclusion and exclusion standards, including gender, age, body mass index (BMI), blood pressure, hospital length of stay (LOS), and hospital costs. Furthermore, the test records of the patients were exported from the LIS system, and the related hematological indicators were recorded, such as fasting plasma glucose, fasting triglyceride, fasting high-density lipoprotein, preoperative and postoperative erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP).

Follow-up was conducted by out-patient consultation or over the phone for 1 year. The Hospital for Special Surgery (HSS) score, which is a measure of alterations in knee functionality, is evaluated (22). The knee function is evaluated on a scale of 100 points, where higher scores indicate better performance. The quality of life in both groups was evaluated using the Short Form [36] health survey (SF-36) score, which consists of 36 items divided into eight dimensions: physical function, role physical, bodily pain, general health, vitality, social function, role emotional, and mental health (23). Physical health is associated with the first four dimensions, whereas mental health is associated with the remaining four dimensions. Prognostic evaluation indicators (postoperative complications, functional and quality of life rating scales) were recorded. Missing data were addressed by casewise deletion.

### Statistical analysis

The statistical analysis was conducted utilizing the IBM SPSS Statistics for Windows, Version 26.0 software (SPSS 26.0). The enumeration data are presented as a percentage, while the measurement data are represented by the mean  $\pm$  standard deviation (SD). The T-test was employed for measurement data that followed a normal distribution, while the rank sum test was utilized for data that did not adhere to a normal distribution. The chi-square test was used to test the counting data. Statistically significant differences were considered when  $P < 0.05$ .

## Results

### Clinical evaluation before the follow-up

There was a total of 227 patients with morbidity TKA, with 83 (36.6%) having MetS and 144 (63.4%) without MetS. The average age of these patients was 68 years, ranging from 47 to 85 years. *Table 1* summarizes the baseline characteristics of the groups with MetS and without MetS. The BMI was divided into two categories: low BMI (BMI  $< 25 \text{ kg/m}^2$ ) and high BMI (BMI  $\geq 25.0 \text{ kg/m}^2$ ) (24). The average BMI and the amount of high BMI cases in the MetS group were considerably greater compared to the non-MetS group. Furthermore, the prevalence of hypertension or diabetes in the MetS group was significantly higher compared to the non-MetS group (both  $P < 0.001$ ). In the MetS group, the triglycerides level was elevated compared to the non-MetS group ( $P = 0.01$ ), whereas the HDL level was decreased in the MetS group compared to the non-MetS group ( $P < 0.001$ ).

The complications after TKA affect the prognosis of patients. There was no significant disparity in the overall occurrence of postoperative complications between the two groups, as indicated by *Table 2*. Furthermore, there was no statistically significant distinction observed in terms of LOS and hospital costs between the two groups. ESR and CRP are frequently utilized indicators of widespread inflammation (25). There was a trend toward MetS patients showing higher postoperative CRP and ESR levels than non-MetS patients, although without statistical significance (*Table 2*).

### Post-follow-up clinical assessment

The analysis focused primarily on examining the improvement of patients' prognosis, specifically the changes in the HSS scores (a scale measuring knee joint health) and SF-36 scores (a scale assessing the quality of life) (*Table 3*). The MetS group had lower HSS knee scores compared to the non-MetS group ( $P = 0.048$ ). The SF-36 scores for each item, except for vitality and social functioning, were lower in the MetS group compared to the non-MetS group during the one-year postoperative follow-up.

## Discussion

The objective of this study was to assess whether the presence of MetS in patients with OA has an impact on the prognosis and quality of life after primary TKA, in

**Table 1** Baseline demographic and clinical characteristics

Variables	MetS OA	Non-MetS OA	P value
Total patients	83	144	
Age (years)	68.72±7.25	67.97±7.39	0.49
Gender			0.92
Male	10 (12.0)	18 (12.5)	
Female	73 (88.0)	126 (87.5)	
BMI (kg/m <sup>2</sup> )	29.10±3.89	25.48±3.30	<0.001
BMI categorized, kg/m <sup>2</sup>			<0.001
<25	9 (10.8)	69 (47.9)	
≥25	74 (89.2)	75 (52.1)	
History of hypertension			<0.001
Yes	41 (49.4)	34 (23.6)	
No	42 (50.6)	110 (76.4)	
History of diabetes			<0.001
Yes	21 (25.3)	3 (2.1)	
No	62 (74.7)	141 (97.9)	
TG (mmol/L)	2.24±1.10	1.51±1.65	0.01
HDL (mmol/L)	1.21±0.25	1.39±2.89	<0.001

Data are presented as mean ± standard deviation or n (%). MetS, metabolic syndrome; OA, osteoarthritis; BMI, body mass index; TG, triglyceridemia; HDL, high-density lipoprotein.

comparison to OA patients who do not have MetS. The knee joint function and quality of life of patients were affected by the MetS groups at the 1-year follow-up. Nevertheless, there were no variations between the groups regarding complications, inflammatory markers, LOS, and hospital costs.

Age, gender, and BMI may impair the prognosis of patients after TKA (26). Most of the participants in this research were senior individuals between the ages of 60 and 75 years. The mean age of individuals in the two groups was 68.72 and 67.97 years, respectively (P=0.49). Moreover, both sets of individuals exhibited identical age distributions. Therefore, age or gender did not account for any of the variations observed among the groups. Different regions of the world share a common denominator in terms of the population of OA. Women have a higher prevalence of knee OA compared to men (27). In this study, the occurrence of OA patients, whether with or without MetS, was considerably greater among females compared to males. The development of knee OA is primarily linked to obesity and

the related MetS (28). In OA patients with a BMI ≥25 kg/m<sup>2</sup>, MetS was present in 89.2%, whereas it was only 10.8% for those with a BMI <25 kg/m<sup>2</sup>. The hospital costs differed based on the patient's age, gender, LOS, occurrence of postoperative complications, and the type of surgery they underwent. The average age and LOS in the two groups were similar in this study. Additionally, the occurrence of postoperative complications was relatively minimal, and both groups underwent the same type of surgery. As a result, there was no notable disparity in the overall hospital cost.

Recent studies have suggested that there is a strong correlation between MetS and low-grade systemic inflammation (29-31). Knee OA is associated with MetS and low-grade systemic inflammation (32). In this study, no significant difference was found yet for the levels of preoperative CRP, ESR, and postoperative CRP, ESR between the two groups. Possible reasons are as follows. First, besides the chronic low-grade inflammation induced by MetS, synovitis is also associated with the intensity and advancement of pain and structural damage in OA (33).

**Table 2** Perioperative information was obtained retrospectively

Variables	MetS OA	Non-MetS OA	P value
Total patients	83	144	
Overall complications	4 (4.8)	7 (4.9)	0.99
Incision infection	2 (2.4)	0	0.06
Anemia	1 (1.2)	2 (1.4)	0.91
Joint effusion	1 (1.2)	3 (2.1)	0.63
Lower-limb venous thrombosis	0	1 (0.7)	0.45
Lower extremity severe pain	0	1 (0.7)	0.45
LOS (days)	12.28±4.28	12.23±4.16	0.93
Hospital costs (RMB)	69,508.3±17,668.7	66,907.7±14,850.5	0.24
Preop-CRP (mg/L)	3.78±8.49	4.30±9.39	0.69
Postop-CRP (mg/L)	31.74±38.85	23.28±24.63	0.09
Preop-ESR (mm/h)	17.10±12.24	17.73±14.89	0.76
Postop-ESR (mm/h)	42.39±31.21	32.33±23.39	0.18

Data are presented as mean ± standard deviation or n (%). MetS, metabolic syndrome; OA, osteoarthritis; LOS, length of stay; Preop, preoperative; Postop, postoperative; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

**Table 3** The knee function and quality of life of the two groups

Variables	MetS OA	Non-MetS OA	P value
Total patients	73	140	
HSS scores	86.84±4.10	88.19±5.03	0.048
SF-36 scores			
Physical function	66.7±8.5	69.6±9.7	0.04
Role physical	57.5±17.5	61.6±15.7	0.09
Bodily pain	85.8±5.0	86.6±7.6	0.39
General health	58.1±9.3	64.6±9.1	<0.001
Vitality	49.1±10.4	47.6±11.5	0.35
Social function	62.8±9.3	59.6±12.4	0.03
Role emotional	60.2±21.0	69.5±21.0	0.002
Mental health	67.9±6.1	70.9±5.8	<0.001

Data are presented as mean ± standard deviation. MetS, metabolic syndrome; OA, osteoarthritis; HSS, Hospital for Special Surgery; SF-36, Short Form [36] health survey.

Additionally, the level of CRP elevation generally reflects the severity of systemic inflammation and disease activity (34). The inclusion criterion was the implantation of a TKA for end-stage knee OA. All patients were at low-grade systemic inflammation regardless of whether they had MetS or not.

Pre-operative levels of inflammatory mediators did not differ between the two groups. Second, all surgeries were performed in the same fashion by the same surgical team in the same institution. There was no notable disparity in inflammation levels in a short time after TKA.

After surgery, patients' knee function was evaluated using the HSS score, where a higher score indicated improved knee joint function (35). HSS is the most commonly and clinically used method. After 1 year of follow-up, our study found that the average HSS score of patients in the MetS group was lower than that of those in the non-MetS group, suggesting that the MetS may have a certain impact on the functional recovery of patients with TKA.

The SF-36 is the most extensively utilized and thoroughly assessed tool for assessing quality of life. The SF-36 is an assessment consisting of 36-item questions that evaluate performance in eight areas. A systematic review has indicated that a substantial body of evidence supports a significant correlation between MetS and the deterioration of quality of life (36). Gholami *et al.* suggested that MetS had an adverse correlation with the quality of life in patients with suspected nonalcoholic steatohepatitis (37). Margiotta *et al.* revealed that MetS affected the quality of life in systemic lupus erythematosus patients (38). Our study found that compared with the non-MetS group, the patients in the MetS group exhibited lower levels of physical function, general health, social function, role emotional, and mental health, which indicated that the OA patients with MetS have inferior physical and mental health compared to those without MetS.

MetS can provide a chronic inflammatory milieu that contributes to the onset of OA. MetS encompasses a range of metabolic abnormalities, including hypertension, hyperlipidemia, and hyperglycemia. The exchange of nutrients within the cartilage may be hindered by subchondral ischemia caused by hypertension, whereas hyperglycemia can result in increased stiffness in the cartilage matrix, degradation of subchondral bone, and dysfunction of chondrocytes (39). Variations in lipid composition may have a significant impact on the modulation of local inflammatory processes and regulation of immune functions, potentially acting as triggering factors for joint lesions (40). The buildup of advanced glycation end products in joints plays a role in the development of cartilage damage in OA (41,42). Li *et al.* demonstrated that MetS worsened the symptoms of pain, depression, and decreased knee function in individuals with OA (18). A study showed that MetS-related factors are associated with worse clinical outcomes after high tibial osteotomy (43). Patients who had MetS have already been shown to have lower scores of HSS and SF-36 after TKA. Therefore, the study on the postoperative knee function and quality of life of OA patients with MetS undergoing TKA treatment is of

great significance for strengthening the understanding of clinical characteristics, improving the therapeutic effect, and then intervening in the etiology at an early stage.

There are certain constraints in the current research. First, it belongs to a single-center retrospective study. Further study will be necessary to determine the generality of this conclusion. Second, this study is retrospective, and the number of patients included is not large. Third, due to the diverse clinical groups in our hospital, it is challenging to comprehensively document all the clinical data of the patients involved in this study. Forth, this study did not compare the preoperative differences between the two groups, as well as analyze the postoperative improvement changes in depth. We will compare the preoperative and postoperative differences between the two groups in more depth in future large sample studies.

## Conclusions

While previous research has identified a higher likelihood of TKA complications in patients with MetS, the current study indicates that MetS might not result in any notable additional complications among individuals with OA. However, MetS may affect the knee joint function and quality of life of patients after TKA.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at <https://aoj.amegroups.com/article/view/10.21037/aoj-24-2/rc>

*Data Sharing Statement:* Available at <https://aoj.amegroups.com/article/view/10.21037/aoj-24-2/dss>

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://aoj.amegroups.com/article/view/10.21037/aoj-24-2/coif>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Clinical Research Ethics Committee of Zhongda Hospital, Affiliated to Southeast University (IRB No. 2020ZDSYLL206-P01) and individual consent for this retrospective analysis was waived.

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