SELÇUK TIP DERGİSİ
SELCUK MEDICAL JOURNAL

Araştırma Makalesi / Research Article

Selcuk Med J 2023;39(4): 157-163
DOI: 10.30733/std.2023.01679

NEÜ YAYINEVİ

Patient Management and Surgical Results in Osteocondroma Cases

Osteokondrom Vakalarında Hasta Yönetimi ve Cerrahi Sonuçlarımız

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Geliş Tarihi/Received: *9 October 2023*
Kabul Tarihi/Accepted: *29 November 2023*

Öz

Amaç: Bu çalışmanın amacı üçüncü basamak bir onkoloji merkezinde cerrahi tedavi uygulanmış osteokondrom tanılı 121 hastanın demografik verilerini, tümörlerin tanı ve tedavi yöntemini ve cerrahi sonrası klinik sonuçlarını sunmaktır.
Hastalar ve Yöntem: 2009-2019 tarihleri arasında osteokondrom tanısı alan ve cerrahi tedavi uygulanan 18-65 yaş arasında olan ve en az 1 yıl takip süresi olan 121 hasta retrospektif olarak incelenerek dahil edildi. Tümör boyutu ve kıkırdak kep kalınlığının herediter tümörü soliter tümörden ayırt etmek için anlamlı cutoff değerlere sahip olup olmadığı ROC analizi ile incelendi.
Bulgular: Hastaların yaş ortalaması 31.7±12,9 yıldı ve %57'si erkektir. Hastaların tümör boyutu ortalaması 43,4 mm ve kıkırdak kep kalınlığı ortalaması 7,1 mm olarak hesaplanmıştır. Ayrıca, çalışmada incelenen hastaların %16,5'inde herediter osteokondrom tanısı, %1,7'sinde ise malign transformasyon sonucu kondrosarkom tespit edilmiştir. Herediter osteokondrom tanısı almış hastaların tümör boyutu ve kıkırdak kep kalınlığı soliter hastalardan anlamlı olarak yüksek bulunmuştur. Tümör boyutu ve kıkırdak kep kalınlığı, herediter tümörleri soliter tümörlerden ayırt etmede kullanılabilecek önemli göstergeler olarak tespit edilmiştir. ROC analizi sonucu kıkırdak kep kalınlığı için kesme değeri 7,5 mm, tümör boyutu için kesme değeri 49 mm olarak belirlenmiştir.
Sonuç: Osteokondrom tedavisi genellikle cerrahi müdahale ile başarılı bir şekilde tedavi edilebilir ve cerrahi sonrası komplikasyonlar nadirdir. Bu çalışma, osteokondrom hastalarının tedavi ve takibinde klinik kararları desteklemek için önemli bilgiler sağlamaktadır.

Anahtar Kelimeler: Osteokondrom, ekzositoz, total eksizyon, kıkırdak kep

Abstract

Aim: The aim of this study is to present the demographic data, diagnostic and treatment methods of tumors, and postoperative clinical outcomes of 121 patients diagnosed with osteochondroma who underwent surgical treatment at a tertiary oncology center.
Patients and Methods: A total of 121 patients between 18 and 65 years of age, diagnosed with osteochondroma and treated surgically, with a minimum follow-up period of 1 year, were retrospectively included in the study between 2009 and 2019. The tumor size and cartilage cap thickness were analyzed with ROC analysis to determine significant cutoff values for distinguishing hereditary tumors from solitary tumors.
Results: The average age of the patients was 31.7±12.9 years, and 57% of the patients were male. The mean tumor size was calculated as 43.4 mm, and the mean cartilage cap thickness was 7.1 mm. In addition, hereditary osteochondroma was diagnosed in 16.5% of the patients, and chondrosarcoma resulting from malignant transformation was detected in 1.7% of the cases. The tumor size and cartilage cap thickness in patients with hereditary osteochondroma were significantly higher than in solitary cases. The tumor size and cartilage cap thickness were identified as important indicators for distinguishing hereditary tumors from solitary tumors. ROC analysis resulted in a cutoff value of 7.5 mm for cartilage cap thickness and 49 mm for tumor size.
Conclusion: Osteochondroma treatment can generally be successfully managed with surgical intervention, and postoperative complications are rare. This study provides important information to support clinical decisions in the treatment and follow-up of osteochondroma patients.

Keywords: Osteochondroma, exostosis, total excision, cartilage cap

Cite this article as: Simsek MA, Yapar A, Atalay IB, Selcuk H, Gungor BS. Patient Management And Surgical Results In Osteocondroma Cases. Selcuk Med J 2023;39(4): 157-163

Disclosure: *None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this article. The research was not sponsored by an outside organization. All authors have agreed to allow full access to the primary data and to allow the journal to review the data if requested.*

INTRODUCTION

Osteochondromas are the most common benign bone tumors. They account for 3% of the general population and make up 20-50% of all benign bone tumors and 10-15% of all bone tumors. Patients usually present with a long-standing, slow-growing, hard, painless, and palpable swelling. (1,2). Osteochondromas are cartilage-capped bony protrusions or exostoses growing outward from the bone surface. The cartilage cap is covered by a fibrous perichondrium with continuity to the underlying bone periosteum (3). They can occur in any bone developing through endochondral ossification. They most commonly occur in the metaphyseal regions of long bones and can rarely occur at the metaphyseal-diaphyseal junction. They commonly affect the areas around the knee and the long bones of the arm and forearm (4). Osteochondromas can have various shapes, such as round pedunculated, mushroom-like, cauliflower-like, horn-like, or sessile. Most osteochondromas are solitary lesions, with Hereditary Multiple Exostosis (HME) accounting for about 15% of osteochondromas (2, 5). Recent studies have indicated that the pathogenesis of hereditary multiple osteochondromas is characterized by genetic mutations. Germ cell mutations in the exostosin 1 (EXT1) and exostosin 2 (EXT2) genes on chromosomes 8 and 11 are associated with the disease (6-8). The cartilage cap in osteochondromas is generally about 2-3 mm thick. In actively growing benign osteochondromas in adolescents, the cap may be 1-3 cm thick. Particularly in adults, a cartilage cap thickness exceeding 2 cm and irregularities in the cap favor secondary chondrosarcoma (9). The most significant findings supporting malignant transformation include sudden rapid growth of the lesion, continued growth of the lesion despite completion of maturation, and pain in the absence of fractures, bursitis, or nerve compression.

In the follow-up radiographs, an increase in the size of the lesion and the presence of pain, along with the presence of amorphous calcification on the graph, erosion of the cartilage septa (10), the development of cartilage cap with a thickness of more than 2 cm on MRI and 1 cm on CT (11, 12), and scattered calcification in the cartilage cap on CT (11, 13) are findings in favor of malignant transformation.

The indicators of the success of surgery and patient characteristics are highly debatable. This is because most studies related to Hereditary Multiple Exostosis (HME) are retrospective, have incomplete information, and have small sample sizes. The purpose of this study is to evaluate the demographic data, diagnostic and treatment methods of benign tumors diagnosed as osteochondroma in 121 patients who underwent surgical treatment.

PATIENTS AND METHODS

This study is a cross-sectional study. A total of 121 patients diagnosed with osteochondroma who underwent surgical treatment between January 2009 and December 2019 at our tertiary oncology center were included. Inclusion criteria were patients between 18 and 65 years of age with a tumoral lesion who were histopathologically diagnosed with osteochondroma and treated surgically by our team, currently alive with at least one year of follow-up at our hospital. Exclusion criteria were as follows patients with pre-diagnosed osteochondroma who did not undergo surgical treatment, patients who discontinued follow-up, patients currently alive but with less than one year of follow-up, patients with histopathology indicating a diagnosis other than osteochondroma, and patients with unavailable follow-up information.

All research data were obtained through examination of patient system records and archive files, and through face-to-face and telephone interviews; no new blood, tissue samples, or imaging tests were requested from any patient within the scope of the research. From the patients' files, age, gender, tumor localization, histopathological diagnosis, preoperative symptoms and duration, applied surgical procedures, presence of recurrence during follow-up, date of diagnosis, date of surgical treatment, and follow-up duration were retrospectively investigated. Institutional Ethics Committee approval was obtained before starting the study (Ethics committee approval number: 2020-12/904). The average tumor size was calculated using macroscopic pathological measurement records and tumor sizes from MRI reports.

Statistical Analyses

The research data were statistically analyzed using the Statistical Package for Social Sciences (SPSS) version 22.0 for Windows. Descriptive statistics were presented as numbers, percentages, mean ± standard deviation, and median (minimum-maximum values) for categorical and continuous variables. The normality of continuous variables was evaluated using visual and analytical methods. Since the data of continuous variables did not follow a normal distribution, the Mann-Whitney U test and chi-square test were used for comparison analysis

between groups for non-normally distributed data and categorical variables, respectively. ROC analysis was used to determine significant cutoff values for tumor size and cartilage cap thickness to distinguish hereditary tumors from solitary tumors. The cutoff point was determined using the Youden index. The level of statistical significance in this study was set at $p \leq 0.05$.

RESULTS

A total of 121 patients, 69 of whom were male, with a mean age of 31.7 ± 12.9 were included in this study. When the distribution of patients' presenting symptoms was examined, 71.9% had swelling, 52.9% had pain, 21.5% had limited mobility, and 17.4% had deformity. Incidental diagnosis was made in 21.5% of the patients (Table 1). The mean follow-up period of the patients participating in the study was 51.3 ± 29.7 months, and 53.7% of the tumors were located on the right side. Most commonly observed localizations were distal femur (32.7%), proximal tibia (15.7%), and proximal femur (8.3%) (Figure 1). The mean tumor size of the patients was 43.4 ± 26.5 mm, and the mean cartilage cap thickness was 7.1 ± 5.1 mm. In terms of hereditary traits, 20 patients (16.5%) were diagnosed with hereditary osteochondroma. Chondrosarcoma resulting from malignant transformation was detected in 1.7% of the patients. When tumor types were examined, 50.4% were pedunculated. Among the 61 patients with pedunculated tumors, the most common types were cauliflower-like (45.9%) and horn-like (32.8%). Only two patients underwent wide resection, while 98.3% underwent total excision. The radiograph and peroperative images of a patient who underwent total excision are presented in Figure 2. The most common reason for surgery was cosmetic (43.8%). Postoperative complications included peroneal nerve injury in one patient. During follow-up, recurrence was observed in three patients (2.5%), and total excision was performed in these cases (Table 2).

There was a statistically significant correlation between tumor size and cartilage cap thickness ($r = 0.642$; $p < 0.001$). There were no significant differences in tumor size and cartilage cap thickness between the pedunculated and sessile tumor groups ($p > 0.05$). The distribution of malignant transformation and hereditary traits among the groups did not show statistically significant differences ($p > 0.05$).

The median age of patients in the hereditary tumor group was 32, while it was 28 in the solitary group, and the ages of the groups were found to be similar ($p = 0.586$). There were no significant differences in gender between the groups ($p = 0.655$). There

Table 1. Demographical and Clinical Features of the Patients

Parameters (N=121)	
Gender, n (%)*	
Male	69 (57)
Female	52 (43)
Age, years	
Mean±sd	31.7±12.9
Median (min-max)	28 (11-70)
Swelling, n(%)	
No	34 (28.1)
Yes	87 (71.9)
Pain, n(%)	
No	57 (47.1)
Yes	64 (52.9)
Deformity, n(%)	
No	100 (82.6)
Yes	21 (17.4)
Incidental, n(%)	
No	95 (78.5)
Yes	26 (21.5)
Neurovascular Involvement, n(%)	
No	119 (98.3)
Yes	2 (1.7)
Movement Limitation, n(%)	
No	95 (78.5)
Yes	26 (21.5)

sd: standard deviation * The percentage of the column has been used

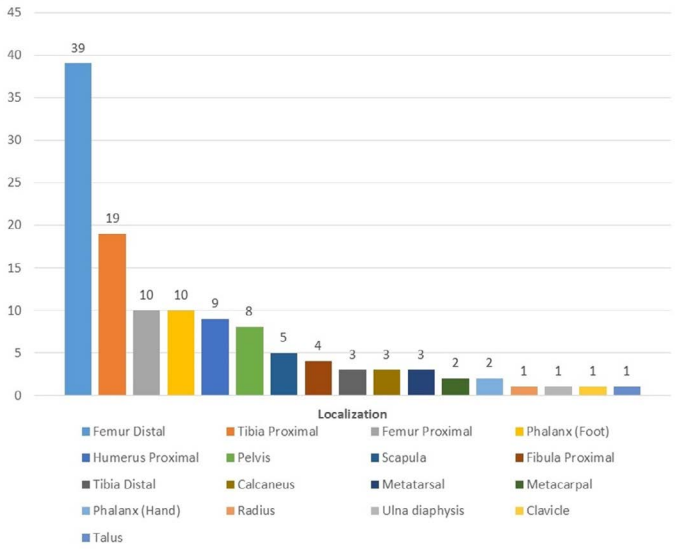

Figure 1. Distribution of osteochondromas by localization

Table 2. Diagnosis and Follow-up Features of the Patients

Parameters (N=121)	
Tumor size, mm	
Mean±sd	43.4±26.5
Median (min-max)	40 (5-130)
Cartilage cap width, mm	
Mean±sd	7.1±5.1
Median (min-max)	6 (1-33)
Familial heritance, n(%)	
Hereditary	20 (16.5)
Solitary	101 (83.5)
Malignant transformation, n(%)	
No	119 (98.3)
Yes	2 (1.7)
Histopathology, n(%)	
Osteochondroma	119 (98.3)
Chondrosarcoma	2 (1.7)
Tumor Type, n(%)	
Pedunculated	61 (50.4)
Sessile	60 (49.6)
Pedunculated tumor shape (n=61), n(%)	
Cauliflower	28 (45.9)
Horn	20 (32.8)
Mushroom	8 (13.1)
Subungual	5 (8.2)
Surgical treatment, n(%)	
Total excision	119 (98.3)
Wide resection	2 (1.7)
Surgical Indication, n(%)	
Cosmetic	53 (43.8)
Pain	34 (28.1)
Movement Limitation	21 (17.3)
Deformity	11 (9.1)
Neurovascular Involvement	2 (1.7)
Postoperative Complication, n(%)	
No	120 (99.2)
Yes (Peroneal palsy)	1 (0.8)
Recurrence, n(%)	
No	118 (97.5)
Yes*	3 (2.5)

sd: standard deviation * 3 patients total excision

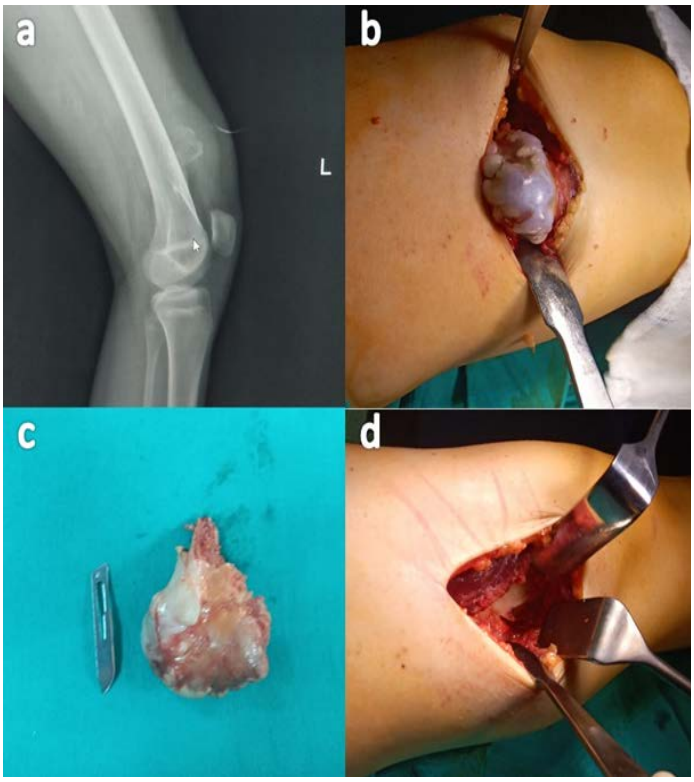

Figure 2. The radiograph (a) and peroperative images (b,c,d) of a patient who underwent total excision

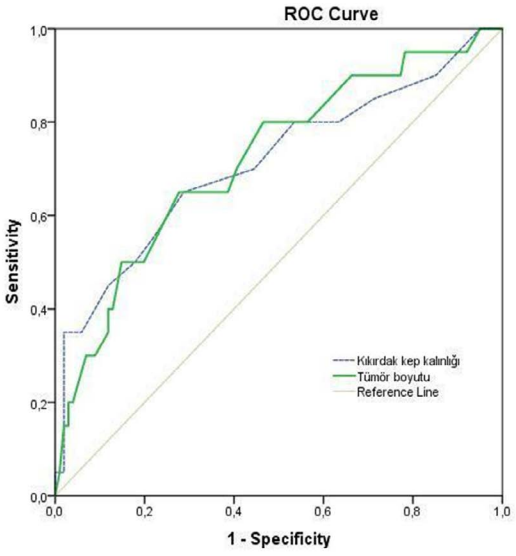

Figure 3. ROC curves pertaining to predictive power of cartilage cap thickness and tumor size for hereditary osteochondroma

were no differences between the groups in terms of follow-up period, surgical treatment, and recurrence status ($p > 0.05$). The median tumor size was 55 mm in the hereditary group and 35 mm in the solitary group. The tumor size of the hereditary group was significantly higher than that of the solitary group ($p = 0.002$). The median cartilage cap thickness in the hereditary group was 9.5 mm, significantly higher than the solitary group's median value of 6 mm ($p = 0.003$) (Table 3). ROC analysis was conducted to test the predictive power of tumor size and cartilage cap thickness in distinguishing the hereditary tumor group from the solitary group. Accordingly, the AUC

Table 3. Comparison of the Hereditary and Solitary Groups

	Familial Inheritance		
	Hereditary (n=20)	**Solitary (n=101)**	**p**
(N=121)			
Age, years			0.586*
Mean±sd	32.5 ±12.2	31.6±13.2	
Median (min-max)	32 (18-64)	28 (11-70)	
Gender, n (%)			0.655**
Male	10 (50)	59 (58.4)	
Female	10 (50)	42 (41.6)	
Follow-up Period, months			0.691*
Mean±sd	48.6±28.9	51.8±29.9	
Median (min-max)	42 (12-120)	48 (12-120)	
Surgical Treatment, n(%)			0.304**
Total excision	19 (95)	100 (99)	
Wide resection	1 (5)	1 (1)	
Recurrence, n(%)			0.421**
No	19 (95)	99 (98)	
Yes	1 (5)	2 (2)	
Tumor Size, mm			0.002*
Mean±sd	62.6±33.7	39.6±23,3	
Median (min-max)	55 (10-130)	35 (5-130)	
Tumor Size, n(%)			0.003**
<49 mm	7 (35)	73 (72.3)	
≥49 mm	13 (65)	28 (27.7)	
Cartilage cap width, mm			0.003*
Mean±sd	11.1±7.5	6.3±4.1	
Median (min-max)	9,5 (2-33)	6 (1-28)	
Cartilage Cap Width, n(%)			0.004**
<7,5 mm	7 (35)	72 (71.3)	
≥7,5 mm	13 (65)	29 (28,7)	
Malignant Transformation, n(%)			0.304**
No	19 (95)	100 (99)	
Yes	1 (5)	1 (1)	
Tumor Type, n(%)			0.237**
Pedunculated	13 (65)	48 (47.5)	
Sessile	7 (35)	53 (52.5)	
Pedunculated Tumor Shape (n=61), n(%)			0.453**
Cauliflower	6 (46.2)	22 (45.8)	
Horn	4 (30.8)	16 (33,4)	
Mushroom	3 (23)	5 (10.4)	
Subungual	0	5 (10.4)	

*1Mann-Whitney U Test **Chi-square Test

Table 4. ROC Analysis Results in Diagnostic Approach to Hereditary Tumor

	AUC (95% CI)	**P**	**Cut-off value**	**Sensitivity (%)**	**Specificity (%)**	**+LHR**	**PPV (%)**	**NPV (%)**	**Max Youden Index**
Cartilage cap	0,712 (0,572-852)	0.003	≥7.5	65	71.3	2.3	31	91.1	0.36
Tumor Size	0,720 (0,593-0,848)	0.002	≥49	65	72.3	2.3	31.7	91.3	0.37

+LHR: Positive Likelihood Ratio, PPV: Positive Predictive Value, NPV: Negative Predictive Value

was 0.720 (p = 0.002) for tumor size and 0.712 (p = 0.003) for cartilage cap thickness (Figure 3). Both variables were found to have the ability to distinguish hereditary tumors from solitary tumors and were statistically significant. The cutoff value for cartilage cap thickness was determined to be 7.5 mm, and for tumor size, it was 49 mm. The sensitivity, specificity, positive predictive value, and negative predictive value for the cutoff values are presented in Table 4.

DISCUSSION

Osteochondromas, or osteochondrogenic exostoses, are the most common benign bone tumors. As they can involve almost the entire skeletal system and are the most common benign bone tumor, they require consideration of various anatomical, surgical, and clinical sensitivities. On the other hand, especially in the hereditary form, such as in the case of multiple hereditary exostoses, the risk of malignant transformation to chondrosarcoma necessitates the establishment of a sensitive clinical examination and follow-up algorithm, despite being benign tumors. This study aims to present data on surgical treatment of patients diagnosed with osteochondroma at a tertiary oncology center. Demographic data of patients, diagnostic and treatment methods of tumors, and postoperative clinical outcomes were evaluated. There are many studies in the literature on the frequency, symptoms, treatment, and outcomes of osteochondromas. The results of this study are considered to be consistent with the literature and may be useful in the management and improvement of surgical outcomes for patients with osteochondroma.

Malign transformation, the most serious complication of osteochondromas, usually occurs within the cartilaginous cap and leads to the development of secondary chondrosarcoma (14). Studies correlating cartilage cap thickness and malignant transformation are available in the literature (1, 9). Cartilage cap thickness greater than 3 cm in children and 2 cm in adults has been reported as a sign of malignancy (15, 16). Studies have indicated that malign transformation occurs in approximately 1% of solitary osteochondromas and 10% of Hereditary Multiple Exostoses (HME) cases (17, 18). In our study, 16.5% of patients were diagnosed with hereditary osteochondroma, and 1.7% were detected to have chondrosarcoma resulting from malignant transformation. No studies were found in the literature that specifically used cartilage cap thickness and tumor size to distinguish between solitary and hereditary osteochondromas. Previous research has shown that the hereditary form of osteochondromas carries a higher risk of malignant transformation (1, 6, 7, 17,18). Therefore, the ability to differentiate between the solitary and hereditary forms of osteochondromas early on is crucial. The findings of our study showed that patients with a diagnosis of hereditary osteochondroma had significantly higher tumor size and cartilage cap thickness compared to solitary patients.

Spontaneous regression has been described in both solitary and multiple hereditary forms in the literature (19). There are two main hypotheses for spontaneous regression. Copeland and Castriota-Scanderbeg suggested that this may occur due to impaired blood supply following repair and remodeling activation after a fracture in the tumor (20). According to this theory, it can be assumed that pedunculated lesions may have a higher likelihood of fractures, and therefore spontaneous regression may be more common in pedunculated lesions. Another theory proposed by Parling et al. is that if the tumor stops growing before skeletal maturation is completed, it will incorporate with the growing metaphysis and undergo resolution (21). In this study, spontaneous regression was not observed in any of the patients during follow-up.

Regarding the timing of surgical treatment, there is no definitive recommendation in the literature. However, in patients with neurological symptoms, surgical decision-making is recommended to be prompt, though not urgent. Generally, there is no evidence that delayed surgery poses a problem in terms of the outcomes of symptoms. There are studies in the literature stating that weakness due to nerve compression continued in the postoperative period, and that early surgery was the correct decision (22,23). Weinar and Hoyt suggested early surgery due to increased anteversion and coxa valga in 25 patients with osteochondromas around the minor trochanter (24).

The limitations of this study include its retrospective design and the fact that it includes data from only a single oncology center, limiting the generalizability of the results. Therefore, larger-scale and prospective studies are needed.

In conclusion, this study provides important information about the management and surgical outcomes of patients with osteochondroma. Moreover, it demonstrates the need for special attention to hereditary tumors and that tumor size and cartilage

cap thickness are important factors for the follow-up and treatment of patients. Lack of sufficient knowledge in this regard can lead to delayed diagnosis and inadequate treatment with serious consequences for the affected patient.

Conflict of interest: *Authors declare that there is no conflict of interest between the authors of the article.*
Financial conflict of interest: *Authors declare that they did not receive any financial support in this study.*

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