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Diagnostic Accuracy of Tru-Cut Biopsy for Soft Tissue Tumors

Yumuşak Doku Tümörlerinde Tru-Cut Biyopsinin Tanısal Doğruluğu

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Abstract / Öz

Introduction: Biopsy is an essential step in the diagnosis of patients with soft tissue tumors. Tru-cut biopsy is a simple procedure that could be performed in the outpatient setting under local anesthesia. It is cost-effective and less time consuming compared with the open biopsy. The aim of the present retrospective study is to assess this biopsy technique with regard to the diagnostic accuracy for soft tissue tumors.

Methods: Patients with suspected soft tissue tumors undergoing tru-cut biopsy and a subsequent tumor resection at our hospital between January 2011 and June 2015 were evaluated retrospectively. Tru-cut biopsy results were compared with the final histopathological diagnosis of the resected tissue specimens. All specimens were routinely stained with hematoxylin and eosin. Immunohistochemistry was performed whenever indicated for differential diagnosis. The sensitivity, specificity, and diagnostic accuracy were calculated and compared using Kappa analysis.

Results: Overall, 41 patients were enrolled in the study. The mean age of the patients was 52.8±16.8 years. Of the 41 patients, 36 had primary soft tissue tumors, and 5 were diagnosed with secondary soft tissue tumors. The diagnostic correlation of the tru-cut biopsy and the resected tissue specimen was 89% (Kappa analysis, $p<0.001$), whereas sensitivity and specificity was 93.3% and 90.9%, respectively.

Conclusion: Tru-cut biopsy is a safe and efficient procedure for the diagnosis of soft tissue tumors. In high grade malignant mesenchymal tumors, the biopsy may not reveal the specific type but may be useful by demonstrating malignant features. In contrast, for low grade, benign, and well-differentiated tumors, a preoperative radiological correlation is essential for the final diagnosis. Although tru-cut biopsy is not diagnostic by itself, it is useful in leading the clinician in the diagnostic pathway. Tru-cut biopsy is a safe, minimally invasive, and time- and cost-effective technique for identifying soft tissue tumors.

Amaç: Biopsi yumuşak doku tümörlerinin tanısında temel adımdır. Tru-cut biopsi lokal anestezi altında ve poliklinik şartlarında uygulanabilen basit bir işlemdir. Tru-cut biopsi, açık biopsiye göre daha az zaman gerektiren ve daha ekonomik bir yöntemdir. Retrospektif çalışmamızın amacı yumuşak doku tümörleri için bu tekniğin tanısal kesinliğini değerlendirmektir.

Yöntemler: Çalışmada hastanemizde Ocak 2011 ve Haziran 2015 tarihleri arasında şüpheli yumuşak doku tümörü nedeniyle tru-cut biopsi uygulanan ve daha sonrasında tümörü rezeke edilmiş olan hastalar retrospektif olarak değerlendirildi. Biopsi sonuçları rezeksiyon materyallerinde verilen nihai kesin tanılarla karşılaştırıldı. Bütün preparatlar rutin olarak H.E (Hematoksilen eozin) ile boyandı. Ayırıcı tanı gerektiren durumlarda tümör örneklerine immünhistokimyasal boyama uygulandı. Sensitivite, spesifite, ve tanısal doğruluk hesaplanarak kappa analizi ile karşılaştırıldı.

Bulgular: Çalışmaya 41 hasta dahil edildi. Hastaların ortalama yaşı 52,8±16,8 yıldı. Otuz altı hasta primer yumuşak doku tümörü ve beş hasta ise sekonder yumuşak doku tümörü tanısı almıştır. Tru-cut biopsi ve rezekte doku örneklerindeki tanısal uyum %89 (Kappa analizi, $p<0,001$), sensitivite ve spesifite sırasıyla %93,3 ve %90,9 olarak bulundu.

Sonuç: Tru-cut biopsi yumuşak doku tümörlerinin tanısında güvenilir ve etkili bir yöntemdir. Yüksek dereceli malign mezenkimal tümörlerinin tanısında biopsi, spesifik tipi belirleyemeyebilir ancak malignite özelliklerinin saptanmasında yararlıdır. Diğer taraftan düşük dereceli, benign, ve iyi diferansiye tümörlerin tanınmasında, preoperatif radyolojik korelasyon esastır. Tru-cut biopsiler tek başına tanısal olmasa bile, klinisyenleri doğru yönlendirmede yararlıdır. Yumuşak doku tümörlerinin tanısında tru-cut biopsi güvenilir, minimal invaziv, zaman açısından tasarruflu ve ekonomik bir yöntemdir.

Keywords: Soft tissue neoplasms, diagnosis, pathology, biopsy, needle

Anahtar Kelimeler: Yumuşak doku tümörleri, tanı, patoloji, biyopsi, iğne

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Introduction

Biopsy is a crucial initial diagnostic step for the identification of soft tissue lesions of the musculoskeletal system (1). Benign and small soft tissue lesions, such as cysts, small lipomas, inflammatory nodules, dermatofibroma, or other benign fibrous lesions, do not require surgical treatment. However, for lesions >4 cm, a histological confirmation is necessary for the diagnosis (2). A fine needle aspiration, tru-cut, or open biopsy may have specific advantages and disadvantages with the aim of obtaining a representative tissue sample with minimal trauma leading to a correct surgical approach for a subsequent resection to facilitate limb-sparing procedures (3).

Open biopsy is the conventional gold standard for obtaining tissue samples for the histological diagnosis. The overall diagnostic accuracy of open biopsies ranges from 91% to 96% (4). Complications of biopsy procedures include seroma, hematoma, infection, wound dehiscence with tumor fungation, and fracture. These complications arise more frequently after open or excisional biopsies. The complication rate of percutaneous techniques ranges from 0% to 1%, whereas the rate is between 4% and 19% for surgical open biopsies (1, 4, 5). Inappropriate biopsy incisions may lead to complications in the subsequent surgical resections, and the high complication rate of an open biopsy procedure affects the treatment plan in 8% of the patients (5).

Fine needle aspiration and tru-cut biopsy have been developed as alternatives to surgical biopsy. These minimally invasive techniques can be easily performed under local anesthesia using computerized tomography, magnetic resonance imaging, or ultrasound (1, 6-9). The accuracy of tru-cut biopsy varies between 76% and 99% (6) and is highly sensitive for primary, locally recurrent, or metastatic lesions in various anatomic locations (10). Despite the reported high accuracy of tru-cut biopsy, majority of the authors focus on the fact that the diagnosis of musculoskeletal tumors requires a team approach with the expertise of the orthopedic oncologist, radiologist, and pathologist. The pathologist's interpretation of the biopsy specimen constitutes the most crucial step in the treatment plan (3, 6).

Cost-effectiveness, avoidance of diagnostic delays, low complication rates, and minimal invasiveness are the advantages of tru-cut biopsy. The potential disadvantages are decreased diagnostic accuracy and possible tumor sampling error. The aim of the present study was to evaluate the accuracy of tru-cut biopsy with regard to its diagnostic yield and to investigate the factors associated with the diagnostic outcomes for distinguishing benign and malignant soft tissue tumors.

Methods

This study was approved by the noninvasive ethical committee of Bağcılar Training and Research Hospital (2015/410). The pathology results of 41 patients (21 females) who underwent a tru-cut biopsy using the tru-cut system (Matek Opticore tru-cut biopsy needle, Matek, İstanbul, Turkey) and received subsequent tumor resection at our hospital, Pathology Department from January 2011 to June 2015 were evaluated retrospectively. All biopsies were performed by an experienced radiologist under ultrasonography. All specimens were fixed with 10% neutral-buffered formalin and processed routinely using hematoxylin and eosin stain for permanent and subsequent immunohistochemical studies performed at the discretion of the interpreting pathologist.

The samples were evaluated by a pathologist experienced in the field of orthopedic oncology and soft tissue pathology. Diagnostic biopsies were analyzed for accuracy with regard to the final histopathological diagnosis of the resected tissue. Reactive and inflammatory soft tissue lesion samples were excluded from the analysis. The final diagnosis was made using the histopathological examination of the resected lesions.

Confirmatory histological specimen reports were available from previous tru-cut histological specimens in one patient presenting with soft tissue masses and from definitive surgical resections. The pathological diagnosis was performed according to the WHO 2013 soft tissue tumor classification system (11). All samples were assessed for the benign or malignant nature of the lesion and for a definite histological diagnosis. Written informed consent was obtained from each patient.

The Statistical Package for Social Sciences software version 22.0 (SPSS Inc.; Chicago, IL, USA) was used for statistical analysis. Tru-cut biopsy and subsequent resection pathology results from were compared. Sensitivity, specificity, and diagnostic compatibility (Kappa analysis) were calculated. A p value less than 0.05 was accepted as statistically significant.

Results

Thirty-six primary and five secondary soft tissue tumors were evaluated in the study based on final diagnosis. The mean age of the patients was 52.8±16.8 years. Tru-cut biopsy was positive for malignancy in 12 patients. Two patients were diagnosed as gastrointestinal stromal tumor (GIST) according to mitosis, location, and size, whereas one patient was diagnosed as high and the other as an intermediate potential risk after the histopathological evaluation of the resected lesions. Two out of four patients with aggressive fibromatosis were misdiagnosed as benign mesenchymal proliferation through tru-cut biopsy (Figure 1). Ten patients had descriptive diagnosis (pieces of lipomatous tissue, connective tissue, skeletal muscle, etc.) through tru-cut biopsy, whereas nine had lipoma and one had xanthoma as the final diagnosis (Figure 2). Of these cases, seven were compatible with lipoma because of preoperative radiological evaluation. One case was equivocal for atypical lipoma through radiological evaluation, and the final diagnosis was fibrolipoma. Another case was evaluated as xanthoma through excisional biopsy, but the previous radiological diagnosis was reported as soft tissue tumor. One patient's diagnosis was vascular neoplasia through tru-cut biopsy, and the final diagnosis was cavernous hemangioma. Two of the primary soft tissue tumors with myxoid features were correctly identified with tru-cut biopsy (Figure 3). We did not observe any significant complications, such as hematoma, infection, or impaired wound healing following tru-cut biopsy.

The tru-cut biopsy and pathological final diagnosis of the resected tissues showed an 89% (Kappa analysis, $p<0.001$) correlation excluding the patients with a descriptive tru-cut biopsy diagnosis. The diagnostic sensitivity was 93.3% and the specificity was 90.9% in our study. The distribution of the lesion sites and diagnoses were highly variable. The patient characteristics, results of tru-cut biopsy, and final diagnosis are shown in Table 1.

Figure 1. Aggressive fibromatosis. Hypocellular tumor composed of bland fibroblasts in the middle and the right sides (case 7; H&E 40X)

Figure 2. This case is diagnosed as a descriptive diagnosis. Skeletal muscle fibers in the left upper and lipomatous tissue fragments in the right and lower quadrant (case 33; H&E 40X)

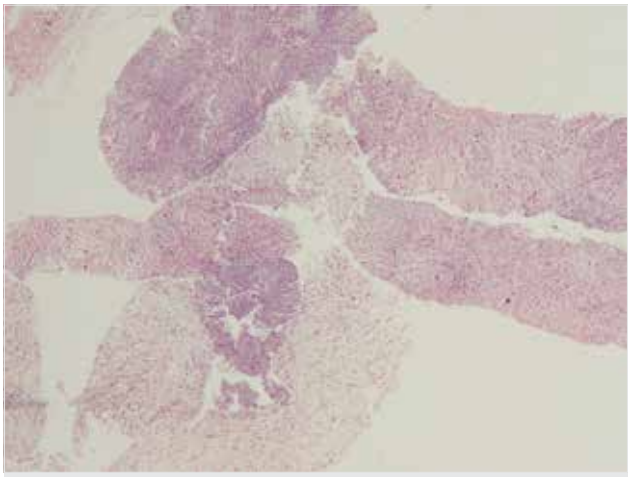

Figure 3. A case of myxofibrosarcoma. Spindle cell mesenchymal tumor containing pleomorphic cells in a myxoid background (case 28; H&E 40X)

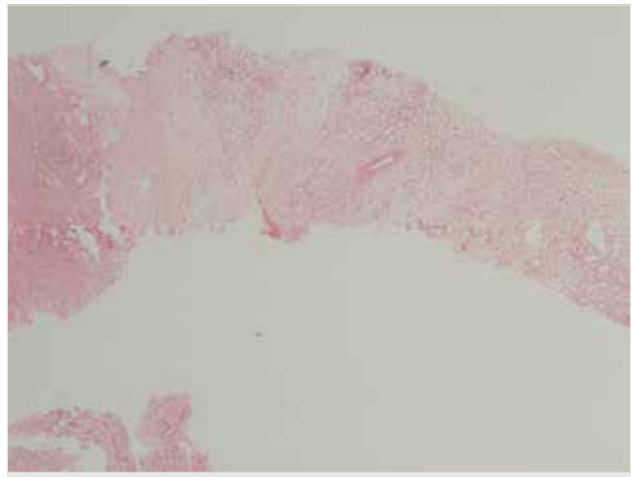

Figure 4. Spindle and focal chronic inflammatory cells in a myxoid and loose stroma. Misdiagnosis is because of sampling from the reactive zone of the adenocarcinoma metastasis (case 40; H&E 40X)

Discussion

A tru-cut biopsy helps reveal the tumor structure and cell configuration and is the fundamental step for the diagnosis of soft tissue tumors. The diagnostic accuracy of tru-cut biopsy has been reported between 69% and 99% (12). The sensitivity ranges between 82% and 95% with a negative predictive value between 76% and 91% (12, 13). The false negative results or diagnostic inaccuracy may depend upon several factors, such as the lesion type, location, experience of the radiologist, and the pathologist. Each of these factors may have comparable influences on the outcome, and false negative biopsies may deleteriously affect the treatment strategy.

In the present study, the sensitivity was 93.3% and the specificity was 90.9%. These findings correlate well with the recent studies. Cooperation of the orthopedist, radiologist, and pathologist may increase the diagnostic yield of tru-cut biopsy because of sampling error, by identifying the convenient or satisfactory tumor area for biopsy. Besides, tru-cut biopsy is a safe technique with a negligible complication rate ranging from 0% to 7.4% in recent studies (14, 15). We did not observe any significant complications associated with the tru-cut biopsy procedure in our patients.

The treatment of soft tissue tumors has focused on limb-salvage surgery during the last two decades. This approach has privileges of accurate diagnosis compared to invasive procedures for guiding the treatment options. Mankin et al. (5) demonstrated a complication rate of 17% for open musculoskeletal biopsies. The complication rate increased two-fold when the biopsy was performed outside of a primary musculoskeletal treatment institution (5). In a multidisciplinary setting of established treating centers for musculoskeletal neoplasms, nondiagnostic tru-cut biopsy and tru-cut biopsy errors can be identified and addressed appropriately without resultant surgical errors (1). The results of our study indicate that the diagnostic utility of tru-cut biopsy highly depends on the multidisciplinary team work of the radiologist, orthopedic surgeon, and the pathologist.

For malignant lesions where a confirmatory diagnostic tissue and features were unavailable, pathologists used immunohistochemistry to confirm the histopathological interpretation and concordant clinical findings to determine the accuracy of the biopsy diagnosis. The lowest diagnostic accuracy rate was obtained with the needle biopsies for myxoid, infectious, and round cell histology lesions (15, 16). Peer et al. (16) have found inconclusive biopsy results for myxoid schwannoma, myxoid liposarcoma, hemangioendothelioma, and lipomatous lesions. Ogilvie et al. (15) revealed a low diagnostic ratio for myxoid lesions. Various studies have also reported that the tumor subtype is the essential dilemma for the interpretation of tru-cut biopsy specimens (2, 15, 17, 18). In our study group, two primary soft tissue tumors with myxoid features were identified correctly as malignant because they had high-grade features. Sung et al. (18) reported a low diagnostic yield and accuracy in heterogeneous tumors, such as angiosarcoma, liposarcoma, synovial sarcomas, and hemangiomas. A case was diagnosed only as a vascular neoplasia in our study because fibrinous deposits and thrombi were present in most of the vascular lumen. Tru-cut biopsy was also diagnostic in a hemangioendothelioma case. As a result, the total excision specimen should be imperative for an adequate identification of the malignancy potential for vascular neoplasia. Mitsuyoshi et al. (17) reported difficulties in differentiating low-grade liposarcoma from benign lipoma. In our study, a descriptive diagnosis was reported for nine cases of benign lipomatous tumors because of the fragments representing the lesion and the surrounding tissues. Consequently, a radiological evaluation appeared imperative as the initial step for the diagnosis of lipomatous tumors. In contrast, lack of atypical histological features supported the benign diagnosis. Malignant and atypical lipomatous tumors were correctly diagnosed using tru-cut biopsy. Three of these cases were well-differentiated liposarcomas and were diagnosed as atypical lipomatous tumor through tru-cut biopsy. A dedifferentiated liposarcoma had been diagnosed as malignant mesenchymal tumor by tru-cut biopsy. Well-differentiated liposarcomas can be diagnosed using tru-cut biopsy with regard to the presence of atypical cellular features, whereas other high-grade malignant mesenchymal tumors should be included in the differential diagnosis of high-grade liposarcomas.

Multiple factors may affect the quality of the guided tru-cut biopsy. Some of these may be lesion specific, such as the tumor type, size, and location, whereas others may be technical in nature, such as the needle size, needle diameter, experience of the clinician, number, and size of the acquired tissue specimens (16). It is well known that as tumors enlarge they may outgrow their blood supply, leading to necrotic areas within the tumor. Sampling of such necrotic areas may lead to inadequate biopsy specimens. The best biopsy samples are typically localized at the margins of the tumor because of the poor diagnostic quality of central tumor mass. One of the secondary soft tissue tumors was diagnosed as a myxoid spindle cell neoplasm, but the final diagnosis of the resected tumor was an adenocarcinoma metastasis (Figure 4). This erroneous diagnosis was because of the sampling of the reactive zone in the peripheral tumor area by tru-cut biopsy. Besides, metastatic tumors are the most frequent secondary soft tissue

Table 1. Characteristics of the patients, lesions, results of the tru-cut biopsy, and final pathological diagnosis

Case #	Age	Diameter	Sex	Tru-cut biopsy diagnosis	Resection-excisional diagnosis
1	56	26 cm	M	Malignant mesenchymal tumor	Dedifferentiated liposarcoma
2	61	U	F	Atypical lipomatous mesenchymal tumor	Liposarcoma (well differentiated)
3	38	12 cm	F	Benign spindle cell proliferation	Aggressive fibromatosis
4	55	8 cm	F	Intramuscular lipoma	Intramuscular lipoma
5	35	21 cm	M	Fibrolipoma	Fibrolipoma
6	83	7,5 cm	F	Pleomorphic malignant tumor	Undifferentiated pleomorphic sarcoma
7	36	5,5 cm	F	Aggressive fibromatosis	Aggressive fibromatosis
8	62	6,5 cm	M	DD	Lipoma
9	38	6,5 cm	M	C with Lipoma	Lipoma
10	54	23 cm	M	Atypical lipomatous tumor	Liposarcoma (well differentiated)
11	74	4 cm	F	Epithelioid hemangioendothelioma	Epithelioid hemangioendothelioma
12	47	15 cm	F	C with Lipoma	Lipoma
13	63	9 cm	M	Lipoma	Lipoma
14	60	5 cm	F	DD	Fibrolipoma
15	27	9,3 cm	F	Benign mesenchymal proliferation	Aggressive fibromatosis
16	83	26 cm	F	Atypical lipomatous tumor	Liposarcoma (well differentiated)
17	46	16 cm	M	Compatible with GIST	GIST
18	24	8 cm	F	Compatible with aggressive fibromatosis	Aggressive fibromatosis
19	54	8 cm	M	DD	Lipoma
20	57	11 cm	M	DD	Angiolipoma
21	79	3,5 cm	F	Schwannoma	Schwannoma
22	68	8 cm	M	GIST	GIST
23	17	22 cm	M	DD	Intramuscular Lipoma
24	66	17 cm	F	DD	Xanthoma
25	55	4 cm	F	Granular cell tumor	Granular cell tumor
26	42	3,5 cm	M	Malignant spindle cell mesenchymal tumor (recurrent tumor)	Clear cell sarcoma
27	50	22 cm	M	DD	Intramuscular Lipoma
28	54	7 cm	M	Myxoid sarcoma	Myxofibrosarcoma
29	46	25 cm	M	DD	Lipoma
30	43	9 cm	M	Compatible with intramuscular lipoma	Intramuscular Lipoma
31	17	4,7 cm	M	Giant cell tendon sheath tumor	Giant cell tendon sheath tumor
32	37	10 cm	F	DD	Fibrolipoma
33	55	9 cm	F	DD	Lipoma
34	15	4 cm	M	Compatible with giant cell tendon sheath tumor	Giant cell tendon sheath tumor
35	73	13 cm	M	C with malignant myxoid mesenchymal tumor	Undifferentiated pleomorphic sarcoma
36	70	7 cm	F	C with vascular neoplasm	Cavernous hemangioma
37	36	5 cm	F	Endometriosis	Endometriosis
38*	66	U	F	Carcinoma	Serous Ca met
39*	57	U	F	Adenocarcinoma met	Endometrioid Ca met
40*	39	17 cm	F	C with malignant myxoid spindle cell neoplasm	Adeno Ca met
41*	66	U	M	Adenocarcinoma met	Colonic adeno Ca met

F: female; M: male; Ca: carcinoma; C: compatible; DD: descriptive diagnosis; U: undetermined; met: metastasis
* Secondary tumors

tumors as it is in our study. These usually may simulate primary soft tissue tumors both clinically and radiologically.

The essential point for a successful tru-cut biopsy in the diagnosis of soft tissue lesions depends upon a careful algorithmic procedure planning by an experienced orthopedic surgeon or a well-trained interventional radiologist in this field with respect to the suspected lesion, extent of necrosis, and the location for avoiding erroneous results or inadequate biopsy specimens (3). Besides its diagnostic facility, tru-cut biopsy is also useful for the treatment strategy including the surgical approach and the neo-adjuvant chemotherapy. The complication rate is even less than 5% when performed by experienced clinicians (5, 19). The most frequent complications are hematoma, bleeding, and infection of the biopsy site. We have not observed any of these complications in our patients.

The limitation of the present study is the small sample size. Further studies with larger populations and heterogeneous tumors are needed to identify the real diagnostic utility of the tru-cut biopsy. Tru-cut biopsy usually allows a definitive diagnosis and is useful for further

treatment strategy options, but its limitations must also be recognized. Clinicians should be aware of the uncertainties of this technique when descriptive diagnosis or nonspecific tissue specimens are reported (20). Our diagnostic criteria fundamentally depend upon the histomorphological, clinical, and radiological features. Because of the presence of heterogeneous features of the soft tissue tumors and particularly the small size of the biopsy samples, diagnosis of such lesions are reported in large category groups, such as malignant myxoid neoplasm or spindle cell malignant tumor. For the evaluation of heterogeneous areas, multiple biopsy samples are needed for tru-cut biopsy. We were unable to perform genetic studies for these patients because we did not have a molecular pathology laboratory. Immunohistochemical staining was used for the differential diagnosis of these lesions.

Conclusion

Although the sample size was small, tru-cut biopsy for diagnosing in soft tissue tumors proved to be a safe and efficient procedure. The diagnostic accuracy of tru-cut biopsy is high. If the procedure is not diagnostic at the initial step, it is useful for leading the clinician in the correct path for the further diagnostic work-up of the patient. Advantages are low cost, avoidance of diagnostic delay, low complication rates, and the small incisions compared to surgical open biopsy. In contrast, decreased diagnostic accuracy because of possible tumor sampling error and tumor heterogeneity may be considered a disadvantage.

Microscopic features of low-grade and well-differentiated tumors, which have an initial descriptive diagnosis by tru-cut biopsy, should be evaluated with preoperative radiological assessment. In high-grade malignant mesenchymal tumors, the biopsy may not reveal the specific type but is useful by identifying the malignant tumors, thereby leading to a correct treatment plan.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethic Commitee of İstanbul Bağcılar Training and Research Hospital (2015/410).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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