Original article

Gamma probe guided surgery for osteoid osteoma: Is there any additive value of quantitative bone scintigraphy?

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A B S T R A C T

Objective: The aim of this study is to evaluate the efficiency of gamma probe guided osteoid osteoma surgery and the applicability of quantitative analyses obtained from preoperative bone scan images.

Material and methods: This study involved 12 osteoid osteoma patients who were treated with gamma probe guided surgery after preoperative bone scan. The calculated contrast ratios between nidus and adjacent healthy bone from preoperative bone scan and the calculated percentages of count reduction after resection of nidus during intraoperative gamma probe application were compared. Patients were followed up for any recurrence or complications.

Results: The mean contrast ratio between nidus and adjacent healthy bone calculated from preoperative bone scan was 43.6% (range 33-53%). Following the nidus excision, an average of 55.8% (range 28-73%) count reduction was estimated with gamma probe in the tumor area. There was no correlation between preoperative scintigraphic contrast ratio and intraoperative gamma probe count reduction ratio (r = 0.46, p = 0.13). Complete cure was achieved in 11 (92%) patients with single operation, during the postoperative follow up period. None of the patients had any major or minor complications during or after the surgery.

Conclusions: Due to high clinical success and low complication rate in osteoid osteoma surgery, gamma probe application is an effective and safe method that should be used more extensively in daily practice.

Cirugía del osteoma osteoid guiada por sonda gammadetectora: ¿existe un valor adicional de la gammagrafía ósea cuantitativa?

R E S U M E N

Objetivo: El objetivo de este estudio es evaluar la eficiencia de la sonda gammadetectora en la cirugía radioguiada del osteoma osteoido y la aplicabilidad del análisis cuantitativo obtenido a partir de las imágenes de la gammagrafía ósea preoperatoria.

Material y métodos: Este estudio incluye a 12 pacientes con osteoma osteoido quienes fueron tratados con cirugía radioguiada por sonda gammadetectora después de la gammagrafía ósea preoperatoria. Se compararon las relaciones de contraste calculadas entre el nidus y el hueso sano adyacente en la gammagrafía ósea y los porcentajes de reducción de cuentas tras la extirpación quirúrgica del nidus. Los pacientes fueron sometidos a seguimiento para detectar recurrencia o complicaciones postoperatorias.

Resultados: La relación media de contraste entre el nidus y el hueso sano adyacente fue de 43.6% (rango de 33-53%). Tras la extirpación del nidus, se estimó mediante la sonda una reducción media de 55.8% (rango de 28-73%) en las cuentas detectadas en el área de tumor. No había ninguna correlación entre ambas relaciones (r = 0.46, p = 0.13). Se alcanzó una curación completa en 11 pacientes (92%) con una única operación, durante el período de observación postoperatorio. Ninguno de los pacientes tuvo alguna complicación menor o mayor durante o después de la cirugía.

Conclusión: Debido a su elevada eficacia clínica y al bajo número de complicaciones quirúrgicas, la aplicación de la sonda gammadetectora en la cirugía del osteoma osteoido es un método efectivo y seguro, más extensivamente en la práctica diaria.

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Introduction

Osteoid osteoma is a benign bone tumor, which mainly affects long bones of children and young adults. This tumor consists of a central round or oval-shaped nidus and a sclerotic bone zone surrounding it.\(^1,2\)

The diagnosis of osteoid osteoma is based on clinical, radiologic and scintigraphic findings. Bone scintigraphy is one of the best methods for the diagnosis of osteoid osteoma and for identifying the precise localization of the nidus.\(^3\)

The treatment of osteoid osteoma is achieved with complete excision or destruction of the nidus. It is difficult to identify the nidus by direct visualization or palpation during operation, therefore intraoperative localization of the tumor is of high importance. Incomplete excision of the nidus may result in recurrence in the post-operation period. Wide resection applied to weight-bearing bones in order to minimize the risk of recurrence may also cause bone weakening and increase the risk of fracture as well.\(^2,3\)

To prevent extensive resection and minimize mortality and morbidity, a precise intraoperative localization of the nidus and confirmation of complete resection is highly important. To serve this aim, several localization methods such as intraoperative nuclear medicine methods, tetracycline fluorescence and imaging-guided methods have been used in practice.\(^1,2,6,7\) Although not very common, gamma probe guided method has been used in patients with osteoid osteoma since 1980.\(^8,9\) Gamma probe is very successful in intraoperative localization of the nidus, which has the highest count measurement.\(^6,7,10\) Nidus localization is followed by the count measurement of the adjacent healthy bone in gamma probe guided osteoid osteoma surgery. This adjacent count value is used as the reference value to terminate the resection, and is regarded as proof of complete resection of the nidus. Nevertheless, the gamma probe counts of nidus and adjacent healthy bone, especially those obtained from lesions that are located in the bone localizations with complex geometric structures may vary widely. This may cause hesitation about the exact localization or about adequacy of excision.

Regarding these findings the aim of our study is to attract attention to gamma probe guided osteoid osteoma surgery, since it is not a widely applied or a well-known method, to find out the efficiency of gamma probe guided osteoid osteoma surgery, and evaluate the applicability of quantitative analyses obtained from preoperative scintigraphic images in order to determine the reference count value to finalize the gamma probe guided operation.

Materials and methods

Patients

Twelve patients with the diagnosis of osteoid osteoma who were treated with gamma probe guided surgery in Kocaeli University Hospital between 2009 and 2011 were analyzed in this prospective study. The study was approved by the institutional ethical committee, and written informed consent was obtained from all the participating patients.

Preoperative diagnostic imaging

Whole body bone scintigraphy was performed in all the patients in order to verify the diagnosis and determine the precise localization of the nidus. Adult patients received intravenous injection of 740 MBq \(^{99m}\text{Tc}\)-methylene diphosphonate (\(^{99m}\text{Tc}\)-MDP), and the children’s doses were adjusted according to their weights. Two-three hours following injections, a whole body scan and static images in anterior and posterior positions were obtained with a two-headed gamma camera system (Infinia, GE Medical Systems, Milwaukee, WI, USA) equipped with low energy, high resolution, and parallel-hole collimators. Thin-section computed tomography was performed in only 8 patients.

Quantification of \(^{99m}\text{Tc}\)-MDP uptake on diagnostic scintigraphy

In the preoperative period, diagnostic scintigraphic images obtained from the gamma camera (GC) were evaluated semi-quantitatively in the anterior or posterior views. Whether anterior or posterior; the image with the highest lesional activity accumulation was used.

On static scintigraphic images, elliptical regions of interest (ROI) of a median size of 2.7 cm\(^2\) were drawn to the area where the nidus was located with the highest point of activity and to the adjacent healthy bone by semi-automatic method. Commercially available software was then used to quantify the maximum of counts within the nidus region (GC N) and the adjacent healthy bone region (GC Adj). In order to estimate the count reduction percentage during gamma probe application, the contrast ratio between the nidus and the adjacent healthy bone was calculated with the following formulation: (GC N – GC Adj)/GC N × 100. However, these calculations obtained from bone scintigraphic images were not used during surgeries.

Gamma probe guided surgery

\(^{99m}\text{Tc}\)-MDP was injected intravenously at the doses used for diagnostic imaging to all the patients approximately 1 h before the surgical procedure. About 15 min after the injection, the skin overlying the nidus where the highest activity accumulation was observed, was marked with permanent ink with the help of a point cobalt–51 source under the gamma camera. Urinary catheterization was performed on the patients with lesions in or around the pelvic area in order to reduce the background activity which may come from the bladder.

All the patients were taken to the operating room for complete excision of osteoid osteoma under general anesthesia. All of the operations in our study were performed by the same surgeon. The surgeon was guided by a nuclear medicine specialist, who was experienced in using the gamma probe, during the operation. A hand-held gamma probe (Crystal Probe 2000, Berlin, Germany) with thallium-activated cesium iodide (CsI:Tl) crystal (diameter 15 mm) was used for the detection and excision of the osteoid osteoma intraoperatively (Fig. 1). The affected bone was reached

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**Fig. 1.** The gamma probe in use during an osteoid osteoma surgery.
Table 1

Demographic, preoperative scintigraphic and gamma probe guided surgical findings.

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age and genre</th>
<th>Loc</th>
<th>Gamma camera counts (maximum count)</th>
<th>Gamma probe counts (counts/s)</th>
<th>Path</th>
<th>FU</th>
<th>Cure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lesion</td>
<td>Adj</td>
<td>Ratio (%)</td>
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<td>Adj</td>
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</table>

Loc: nidus location; Adj: adjacent; Path: pathologically confirmed; FU: follow up (months); Fp: femur proximal; Fd: femur diaphysis; Td: tibia diaphysis; Ac: acetabulum.

with an incision through the previously marked skin area. The nidus with the highest activity accumulation was determined by slowly moving the gamma probe along the surface of suspected bone area (GP N). Then, the counts were obtained from the adjacent healthy bone by the gamma probe (GP Adj). Counts of nidus and adjacent healthy bone were measured in counts per second and recorded. The nidus determined by the guidance of the gamma probe was excised intralesionally.

The surgical excision was completed when gamma probe counts obtained from excised nidus area (GP AE) became equal or lower to the counts obtained from the adjacent healthy bones. In most of the cases, the nidus was taken out in multiple small fragments; therefore ex vivo gamma probe counts were not evaluated. The histopathologic evaluations of the excised bones were performed. Following surgery, count decrease percentages of the tumor area after excision were calculated with a formula \((\text{GP N} - \text{GP AE})/\text{GP N} \times 100\) in all the patients. During the follow-up period, the recurrence patterns or any complications were also evaluated.

Analysis

All the statistical analyses were performed by using SPSS version 16.0 for Windows (SPSS Inc., Chicago, USA). Demographic and clinical features of the patients were reported as mean ± standard deviation, median, and percent (%). Distribution of the data was determined to be normal with the Kolmogorov-Smirnov test. Correlation analysis between the contrast ratio values calculated from preoperative diagnostic scintigraphic images and the actual gamma probe count decrease percentage values were performed by using Pearson’s linear correlation test. p values lower than 0.05 were considered statistically significant.

Results

Patient demographics

Of 12 patients, eight patients were male and four patients were female. Half of the patients were in pediatric age. The ages of the patients varied from 8 to 43 years with a median age of 17 years.

Preoperative imaging findings

The nidus of the osteoid osteoma was successfully determined by focally increased uptake in preoperative bone scintigraphy in all of the patients. The localization of osteoid osteoma was in the proximal femur in 8 (67%) patients, in the diaphysis of femur in 2 (17%) patients, in acetabulum in 1 (8%) patient and in the diaphysis of tibia in 1 (8%) patient. The mean contrast ratio between nidus and adjacent healthy bone measured from preoperative scintigraphic images was 43.6% (range 33–53%) (Table 1). Median time interval between preoperative whole body bone scintigraphies and gamma probe-guided surgeries were 14 days (range 5–19 days). CT was used to localize the tumor in eight patients and successfully identified the nidus in all of these cases. The mean tumor size was 10 mm (range 5–15 mm).

Gamma probe guided surgery findings and clinical outcome

Following the nidus excision, a mean count reduction of 55.8% was estimated with gamma probe in the excised tumor area. Bone grafting or internal fixation was not required in any patient, and all the patients were mobilized in the early postoperative period (1–2 days). On histopathological examination, the nidus could be determined only in 7 of the patients’ specimens (58%). Neither nidus nor other pathological entity was histologically found in the remaining patients. None of the patients had major or minor complications during surgery and all of the patients were followed up for any recurrence and complications postoperatively.

During a median follow-up period of 20.5 months (range: 6–34 months), eleven of the patients (92%) had reported complete relief of pain. The recurrence was observed in only one patient who was 8 years old. The recurrent tumor was localized in the acetabular region (Fig. 2). Because of continuous and severe pain, she was re-operated with conventional surgery for osteoid osteoma following 6 months after the first operation and the cure was achieved (Table 1).

Concordance of findings between gamma probe guided surgery and preoperative scintigraphic imaging

There was no significant correlation between the calculated nidus/perinidal healthy bone contrast ratio obtained from preoperative diagnostic scintigraphic images and the count reduction ratio after resection obtained intraoperatively with gamma probe \((r = 0.46, p = 0.13)\).

Discussion

Osteoid osteoma is a benign bone tumor with a nidus of less than 2 cm, mostly located in long bones especially proximal parts of the femur and most of the cases are under 20 years of age with a significant male predominance. \(^\text{1,2,11}\) Similar to these findings, most of the patients in our study were also children or young male adults, the tumors were most frequently located in the femur and the tumor sizes were ranging from 5 mm to 15 mm in whom CT was performed.

Radiography, computed tomography, magnetic resonance imaging and bone scintigraphy are the methods to diagnose and determine the location of osteoid osteoma. The standard treatment for osteoid osteoma is surgery. The aim of the surgery is to excise the nidus completely by conserving the surrounding sclerotic bone. After the excision of the nidus, there is a permanent pain relief during the early recovery period and continuous pain is an indicator of an incomplete excision.1,2,5,11,12 Therefore, localization of the nidus is the key factor that determines the success of the surgery. In all of our cases, osteoid osteomas were diagnosed and localized successfully by bone scintigraphy.

Several surgical methods are used in osteoid osteoma surgery. The most favorable method used in the past was wide en bloc resection of the tumor. This traditional method, that includes the resection of both the nidus and the surrounding reactive tissue, is still used by many medical centers. Wide resection, made in order to reduce recurrence rate, also weakens the bone dramatically and causes a significant increase of morbidity. Bone grafting, internal fixation or long-term immobilization may be required to reduce the risk of pathological bone fracture after the application of this technique.1,2,13–17

Since 1980, some new less invasive surgical techniques have initiated as an alternative to conventional surgery. Burr–down technique, intralesional excision by gamma probe or portable gamma camera guidance, CT-guided percutaneous drill excision, laser photocoagulation, thermocoagulation, radiofrequency ablation are among these techniques.11,13,18,19 Nidus is completely excised or destroyed without disrupting the surrounding reactive tissue by these techniques. In order to locate the nidus precisely, methods such as landmark determination from preoperative images, CT-guided wire marks made on the nidus, tetracycline fluorescence and intraoperative nuclear medicine techniques may be used.1,2,4,11,14,20 Today, CT-guided percutaneous procedures, especially radiofrequency ablation, where the lesion is destroyed by using a drill or trephine are the procedures that are the most popular and are getting more and more favorable.19,21 The success rate of these percutaneous procedures may vary from 73 to 100%.17 On the other hand, this technique has some limitations like the difficulty of application in lesions in superficial locations, where there are neighboring joints or in lesions that are close to important vascular or neurological structures.19,22–24 Moreover, complication rates ranging between 0 and 24% were reported in the literature after percutaneous procedures such as neurological and vascular deficits, muscular hematomas and osteomyelitis.19,21–27

Parallel to the increase in the number of centers that have gamma probe device, there has been an increase in the use of intraoperative gamma probe especially in determining sentinel lymph node and in parathyroidectomy surgery. However, this technique has not been popularized by the orthopedists in osteoid osteoma surgery. There are also a limited number of studies in the literature about the guidance of gamma probe in osteoid osteoma surgery.6–8,10,14,18,28–30 Since osteoid osteomas accumulate the bone seeking radiopharmaceuticals invariably in a specific way, by the help of intraoperative gamma probe, the nidus where maximum signal is delivered can be identified precisely and easily. In addition, count intensity of the tumor after intralesional excision revealed a significant decrease or equalized the rate of the adjacent healthy bone, thereby confirming complete removal of the nidus. With this less invasive technique, extent of the resection is kept in the least minimum limits, and thus, there is no significant weakness in the bone. Early functioning is possible by this technique without any need for a bone graft or the placement of implants. The ideal site for the surgical incision can be determined by marking the lesion overlying the skin with the help of gamma probe or preoperative scintigraphic images, and the bone is reached only with a little incision. Compared to other nidus localization techniques, lesion is localized faster, and the surgery duration is by skin marking and using gamma probe together.14,28,30 In addition, this technique minimizes the need for intraoperative X-ray use, and compared with CT-guided procedures, patients are exposed to less doses of radiation.29 Shorter operation times, little incision and less resection result in early postoperative recovery. Confirming these findings, none of the patients in our study required any graft or implant application and no major or minor complications were observed during or after the surgery. On top of all this, a 92% success rate was obtained in gamma probe guided surgery and a decrease of gamma probe count rate varying from 28% to 73% was determined. If we compare the results of conventional open surgery in the literature with our results, it can be clearly seen that intraoperative gamma probe technique is far more successful in terms of both outcome and complications. In accordance with our findings, success rates varying from 86% to 100% and a 20% to 84% decline in gamma probe measurements were reported for appendicular skeleton, spinal and cranial lesions in similar studies in the literature.6–8,14,15,18,28–30 These decline ratios in the gamma probe count rates may vary widely depending on the radiopharmaceutical injection time, the thickness of the bone and the uptake of the perinidal healthy bone. The contrast ratio obtained from preoperative diagnostic scintigraphic images varied from 33% to 53% in our study. In the case of the child with osteoid osteoma of the acetabulum where the gamma probe surgery failed, this rate was 33%, which was the lowest among all other patients. The complex geometrical structure of the acetabulum and low nidus/perinidal...
healthy bone contrast due to high epiphysis activity are believed to be the causes of the failure of the procedure. The gamma probe procedures in the literature reported increasing failure rates especially in sites showing complexity like acetabular region and in lesions of children located in the epiphysis where high physiological healthy bone activity accumulation is observed.14

High and variable gamma probe counts around tumor site can be measured in tumors that are localized in sites with complex geometric structures and in the epiphysial regions of pediatric patients. In those cases, it is difficult to localize the nidus with a gamma probe in the correct way. Different measures obtained from adjacent healthy bone area at the same time, may cause hesitation about the operation completion reference value and the sufficiency of excision as well. The researchers in this study aimed to find out the contrast rate of the nidus and the adjacent healthy bone area obtained from preoperative diagnostic scintigraphic images, the decline in the count rate by gamma probe during the operation and finally to find out the gamma probe reference value for the operation completion. However, no statistical correlation was found between the preoperative and intraoperative rates. Similar to our findings, Wioland and his colleagues were not able to find any correlation between gamma probe-guided operation analyses and nidus-to-healthy bone uptake ratio obtained from preoperative diagnostic scintigraphic images.14 The differences between gamma probe and gamma camera crystal structure, the time delay differences between injection and imaging, distance differences of lesions to crystals and the lower attenuation of the soft tissue in gamma probe application may be the causes of these non-correlative results.

Although 92% of the patients in our study reported complete relief of pain, only 58% of the patients’ histopathological examination confirmed osteoid osteoma which is believed to be related with the excision of the pathological bone in multiple small fragments in most of the cases. The similar results are also reported in some studies in the literature in which nidus can not be shown histologically.6,31,32 This technique has an important disadvantage of requiring double radiotracer administration. Nevertheless, a same day approach could be performed to avoid a second radiotracer administration, especially in pediatric patients. In addition, this technique requires a learning curve for the surgeon in order to get oriented to the gamma probe device and the preoperative scintigraphic images. However, since the technique and operating the device is not complicated, this learning period is not long and the guidance of a nuclear medicine specialist in the procedure can facilitate the adaptation period.

The most striking limitation of this study is the limited number of patients and the localization of the lesions mostly in the femur.

Conclusion

As a result, gamma probe procedure is a highly effective, safe and less invasive technique which both enhances the localization of the nidus and facilitates the verification of complete resection, especially applicable in cases with a high contrast ratio in preoperative diagnostic scintigraphic images. Intraoperative gamma method should be kept in mind as a reliable alternative method where there is a lack of equipment for percutaneous procedures or where other methods are not convenient. No clinical benefit could be observed in the application of preoperative scintigraphic quantitative analyses in gamma probe procedures. Nevertheless, alternative surgical procedures can be an option in cases where the contrast ratio between the nidus and the adjacent healthy bone region in diagnostic scintigraphic studies is observed to be very low due to the location of lesions in sites with complex geometrical structure, taking the low efficiency of gamma probe application into account.

Conflict of interest

The authors declare no conflict of interest.

References
