

EFFICACY OF THE ENNEKING STAGING SYSTEM IN RELATION TO TREATING BENIGN BONE TUMORS AND TUMOR-LIKE BONE LESIONS

José Marcos Nogueira Drumond

ABSTRACT

Objective: To evaluate the efficacy of the Enneking staging system for determining the prognosis, planning surgical treatment and indicating adjuvant therapy for benign bone tumors (BBT) and tumor-like bone lesions (TBL). *Methods:* A retrospective multicenter, descriptive, nonrandomized study was carried out on a representative sample comprising a large series of 165 patients with a total of 168 benign bone tumors and tumor-like bone lesions. The patient sample was typical, and matched the literature in all respects. All the patients were classified according to the Enneking staging system, and the initial staging of each lesion was correlated with its behavior after either conservative or surgical treatment, in order to determine the efficacy of the system. The treatment options and complications were described and analyzed. *Results:* The results from the treatment provided 95.2% agreement with the Enneking staging system, with a 95% confidence interval of between 90.8 and

97.9%. Of the 168 tumors treated, only eight (4.8%) could not be controlled in relation to the initial treatment indicated by the Enneking staging system. Tumors classified as active were the most prevalent, comprising 73.2% of the lesions. Tumor recurrence was significantly more frequent ($p < 0.001$) in the aggressive stage. All the patients staged as latent evolved to cure. The study suggested that surgery with wide margins, for aggressive lesions, could provide better lesion control, with a lower recurrence rate ($p > 0.001$). For latent and active lesions, the study demonstrated the efficacy of both expectant treatment and excision, with or without autogenous bone graft. *Conclusion:* The results confirm that the Enneking staging system was very efficient in determining the prognosis, enabling surgical planning and indicating adjuvant therapy for treatment of BBT and TBL.

Keywords – Bone diseases; Bone neoplasms/diagnosis/epidemiology/pathology/radiography/surgery; Neoplasm staging

INTRODUCTION

Benign bone tumors and tumor-like bone lesions are relatively rare diseases that mainly affect children and young adults, whose skeleton is still undergoing formation. These diseases can cause fractures, bone and joint deformities and gait disorders, and sometimes leave disabling sequelae for life.

Once the tumor has been diagnosed, it must be staged with a view to treatment. Enneking was the first to describe a staging system for benign bone tumors and nowadays this is the most commonly used system⁽¹⁻⁵⁾.

This staging system introduced a unique language to evaluate and compare the results from different patient protocols and patient series from different treatment centers.

By linking the tumor stage to surgical margins, the surgical procedure indicated for achieving control and cure for the lesion can be obtained^(3,4).

The Enneking staging system was published in the 1980s⁽¹⁻⁵⁾ and studies are needed to test it, verify its efficacy and refine it⁽⁶⁾ (Table 1).

The objective of this study was to evaluate the efficacy of the Enneking staging system for determining the prognosis, planning surgical treatment and indicating adjuvant therapy, in order to manage benign bone tumors and tumor-like bone lesions.

METHODS

A descriptive observational study was carried out on a large series of cases. The study was nonrandomized,

MSc in Health Sciences from IPSEMG, Belo Horizonte; Orthopedist at IPSEMG, FHEMIG and the Orthopedic Hospital, Belo Horizonte, MG, Brazil; Head of Service at FHEMIG (Hospital Foundation of the State of Minas Gerais).

Work performed at IPSEMG (State Employees' Social Security Institute of Minas Gerais), Belo Horizonte
Correspondence: Rua Prof. Estevão Pinto, 555/304, Serra, 30220-060 Belo Horizonte, MG. E-mail: jmnd@uai.com.br

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Table 1 – Enneking staging system: linkage between stages and surgical margins

Tumor stage (benign)	Grade, location, metastases	Clinical evolution	Control margin
1	GoToMo	Latent	Intracapsular
2	GoToMo	Active	Marginal or intracapsular plus effective adjuvant
3	GoT _{1,2} M _{0,1}	Aggressive	Wide or marginal plus effective adjuvant

Go = Benign, To = Intracapsular, T1 = Extracapsular, Intracompartmental, T2 = Extracapsular, Extracompartmental, Mo = Absence of metastases M1 = Presence of metastases.

retrospective and multicenter. The data were gathered by the author from medical records and imaging examinations on patients treated at the IPSEMG Hospital, the Orthopedic-AMR Hospital, the Belo Horizonte Hospital and the São Francisco de Assis Hospital, all in Belo Horizonte, Minas Gerais. The imaging exams consisted of simple radiographs, computed tomography, nuclear magnetic resonance, scintigraphy and arteriography. The sample was formed by 165 patients, with 168 tumor lesions, who underwent either outpatient conservative treatment or hospital surgical treatment (Tables 2 and 3).

Table 2 – Benign bone tumors

	Number of patients
Osteochondroma	31
Enchondroma	14
Giant cell tumors	13
Chondroblastoma	12
Osteoid osteoma	10
Chondromyxoid fibroma	2
Intraosseous lipoma	2
Benign fibrous histiocytoma	1
Total	85

Source: SAME HGIP, HO, HBH, HSF, 2008.

Table 3 – Tumor-like bone lesions

	Number of patients
Non-ossifying fibroma	25
Simple bone cyst	19
Fibrotic dysplasia	17
Aneurysmatic bone cyst	10
Ossifying myositis	6
Hyperparathyroidism	3
Total	80

Source: SAME HGIP, HO, HBH, HSF, 2008.

One patient with multicenter giant cell tumor presented four lesions. Among the patients with osteochondroma, there were four cases of osteochondromatosis. Only one patient, with giant cell tumor, presented lung metastases. These were patients treated consecutively by the author over a 16-year period, between January 1988 (which was when the Enneking staging system came into use) and January 2004. For patients to be included in the study, the minimum length of follow-up required was three years.

The patients' mean age was 23.2 years. The youngest patient was three years old and presented osteoid osteoma, and the oldest was 69 years old, presenting enchondroma. There were 82 male patients and 83 female patients. The femur was the bone most affected, accounting for 40% of the lesions, followed by the tibia, with 20%. Other highly affected bones were the humerus, fibula, iliac and radius. The maximum length of follow-up was 19 years and the minimum was three years, with a mean of 8.35 years.

Considering the stages, 36 patients were latent (B1), 123 were active (B2) and nine were aggressive (B3). Among the aggressive ones, five were giant cell tumors and four were aneurysmatic bone cysts.

Thirty-nine tumors were treated conservatively and another 129 were treated with surgically. Adjuvant therapy was used for 30 tumors, using polymethylmethacrylate (PMMA) cement in 29 cases and radiotherapy in one.

The conservative treatment consisted of clinical-radiological observation in 29 cases and immobilization with plaster casts for fractures in ten cases. The surgical treatment followed the linkage between the stages and the surgical margins of the Enneking staging system (Table 1). The treatment methods are described in Table 4 and the surgical margins that were used are described in Table 5.

Widening the margin using a high-speed rotary drill was carried out in all the cases of intralesional excision, as well as electrocauterization of the cavity. In six cases, multiple Kirschner wires were inserted into the cementation. Autogenous iliac bone grafts was used in 29 cases and homologous grafts in two cases. Bone slippage was performed in one case. One patient with a pelvic aneurysmatic bone cyst was treated with selective arterial embolization and radiotherapy. Anatomopathological examinations were performed on all the patients who underwent open treatment.

Table 4 – Surgical treatment methods

Type	Number of cases
Simple excision	40
Excision and bone graft	31
Excision and cementation	29
Biopsy alone	8
Infiltration with corticoid	8
Osteosynthesis	7
Joint prosthesis	5
Segmental excision	3
Arthrodesis	1
Total	132

Source: SAME HGIP, HO, HBH, HSF, 2008.

Table 5 – Surgical margins used

Type	Number of cases
Intracapsular	53
Marginal	71
Wide	5
Total	129

Source: SAME HGIP, HO, HBH, HSF, 2008.

All the patients were staged using the Enneking staging system and the treatment performed, surgical margins obtained and whether any adjuvant was used were identified. The date when treatment started was also determined, together with the minimum follow-up of three years, treatment results and presence of relapses and cure. Subsequently, a correlation between the initial staging of each lesion and its behavior during the follow-up was made in order to determine the efficacy of the Enneking staging system for predicting the prognosis, planning the surgical treatment and indicating adjuvant therapy.

The criterion for determining whether cure was achieved was the clinical-radiological condition after three years of follow-up. To verify relapses, imaging examinations or anatomopathological examinations after reoperation were used.

For a population to be considered large, the sample requires 141 patients. With a sample of 165 individuals, medium effect, significance level of 5% and two degrees of freedom, the power of this study was 94%. With only one degree of freedom, the power was 97%.

The statistical analysis consisted of the chi-square test, Fisher's exact test and calculation of the confidence intervals for the percentage of agreement. In all the analyses, the significance level was taken to be 5% or 0.05.

A bibliographic review was conducted in the Medline and Lilacs databases was carried out over a ten-year period, between January 1997 and December 2006. In total, 450 abstracts on this topic were found, from which 100 studies with the complete text were chosen. These studies presented the best methodologies and levels of scientific evidence. In addition to these texts, the classic studies on this topic were selected, regardless of the publication date.

The present project was approved by the Research Ethics Committee of the IPSEMG Hospital (HGIP).

RESULTS

The results from the treatment showed a high percentage of agreement with the Enneking staging system, with regard to three parameters of determining the prognosis, surgical planning and adjuvant therapy (Table 6).

Table 6 – Agreement between the treatment results and the Enneking staging system (ESS) in relation to the prognosis, surgical planning and adjuvant therapy.

ESS	Prognosis		Surgical planning		Adjuvant therapy	
	n (1)	%	n	%	n	%
Yes	160	95.2%	121	93.8%	26	86.7%
No	8	4.8%	8	6.2%	4	13.3%
Total	168	100.0%	129	100.0%	30	100.0%

(1) n = Number of cases

The overall analysis, including all the tumors, showed an agreement rate of 95.2% between the treatment and the Enneking staging system, with a 95% confidence interval for this proportion that ranged from 90.8 to 97.9% (Table 7 and Figure 1).

The final results from the treatment showed that out of the 168 tumors treated, only eight (4.8%) were not brought under control with the initial treatment indicated by the Enneking staging system (Table 7). Clinically, out of the 165 treated patients, 159 were cured or became asymptomatic, four presented symptoms and two died.

Table 7 – Agreement between the treatment results relating to benign bone tumors and tumor-like bone lesions and the Enneking staging system (ESS)

ESS	Benign bone tumors		Tumor-like bone lesions		Total	
	n (1)	%	n	%	n	%
Yes	85	96.6%	75	93.8%	160	95.2%
No	3	3.4%	5	6.2%	8	4.8%
Total	88	100.0%	80	100.0%	168	100.0%

(1) n = Number of cases

Group	Agreement proportion	95% confidence interval for the proportion (%)
Benign bone tumors	96.6	90.4 – 99.3
Tumor-like bone lesions	93.8	86.0 – 97.9
Total	95.2	90.8 – 97.9

Note: By definition, the confidence interval for a proportion is not symmetrical around the estimated value for the proportion, as it would be in the case of a confidence interval for a mean

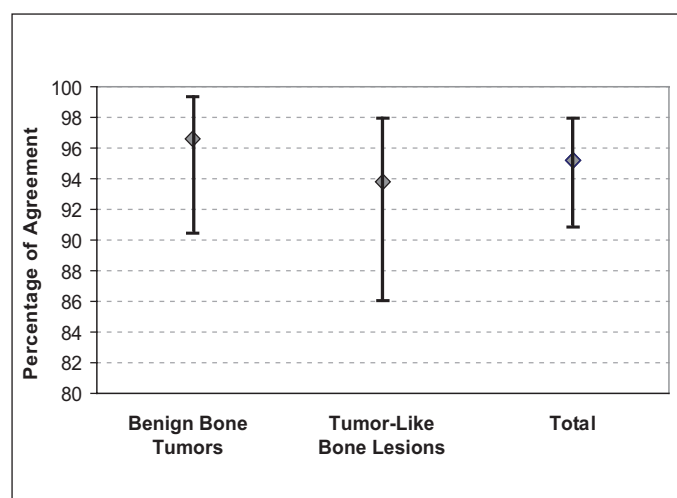


Figure 1 – 95% confidence intervals for the estimated percentage agreement in each group

When dividing the tumors according to stages, the active type (B2) predominated, with 73.2% of the lesions, leaving the latent stage (B1) with 21.4% and the aggressive stage (B3) with 5.4%, as shown in Table 8. In this study, simple bone cysts were responsible for more than 50% of the diagnoses that were made due to a pathological fracture, followed by non-ossifying fibroma and fibrotic dysplasia.

Out of the 129 patients who underwent surgery, there were eight relapses (four B2 and four B3), as shown in Table 9, and an overall rate of 6.2% (Table 6).

The relapses were more frequent in the aggressive stage (B3) with a rate of 44.4% (four out of nine patients). Giant cell tumors were included among these, with three relapses staged as B3, out of 16 treated tumors, resulting in a rate of 18.75%. No active (B2) giant cell tumor relapsed. For patients with operated giant cell tumors by means of marginal surgery and cementation, the relapse rate was 30% (three B3 cases from a total of ten). These three patients were operated again. One underwent wide surgery, had a shoulder endoprosthesis implanted and achieved cured. Another presented a second relapse in marginal surgery with cementation and then a third relapse and was lost from the follow-up after wide surgery and replacement with a fibular graft for a distal tumor of the radius were indicated. The third patient presented primary malignant transformation to femoral fibrosarcoma and was treated with a femoral endoprosthesis.

The four B2 tumors that relapsed (rate of 3.3%; four out of 123 cases) presented simple bone cysts of the femoral neck, fibrous dysplasia of the humeral diaphysis, dysplasia of the femoral neck and aneurysmatic bone cyst of the femoral neck (Tables 8 and 9). All of these patients underwent reoperation and were cured by means of intracapsular surgery and autogenous bone grafts.

Table 8 – Agreement according to stages, between the treatment results and the Enneking staging system (ESS)

ESS	Latent		Active		Aggressive		Total	
	n (1)	%	n	%	n	%	n	%
Yes	36	100.0%	119	96.7%	5	55.6%	160	95.2%
No	0	0.0%	4	3.3%	4	44.4%	8	4.8%
Total	36	100.0%	123	100.0%	9	100.0%	168	100.0%

(1) n = Number of cases

The earliest relapse occurred after six months and the last was after five years, with a mean of 23.75 months for the eight relapsed cases (Table 9).

All the patients staged as latent (B1) evolved towards cure, with a rate of 100% (Table 8).

The adjuvant therapy with PMMA cement presented only three relapses (10.3%) out of 29 operated cases. The three tumors were giant cell tumors staged as B3.

Table 9 – Relapses

Name	Type	Gender	Age	Staging	Surgery	Relapse
1. RDS	GCT	M	19	B3	Marginal (proximal humerus) + PMMA adjuvant	14 months
2. DSG	GCT	M	27	B3	Marginal (distal radius) + PMMA adjuvant	11 months
3. GGT	GCT	F	38	B3	Marginal (distal femur) + PMMA adjuvant	6 months (malignant transformation)
4. BHOM	SBC	M	5	B2	Intracapsular (femoral neck)	17 months
5. AJT	FD	F	23	B2	Intracapsular (femoral neck) + autogenous bone graft	48 months
6. ASS	FD	F	32	B2	Intracapsular (humerus diaphysis) + autogenous bone graft	22 months
7. CCCR	ABC	M	5	B3	Intracapsular (iliac wing) + embolization + radiotherapy	60 months (malignant transformation)
8. RCB	ABC	M	10	B2	Intracapsular (proximal femur) + autogenous bone graft	12 months

Source: SAME HGIP, HO, HBH, HSF, 2008.

PMMA = Polymethylmethacrylate; GCT = Giant cell tumor; SBC = Simple bone cyst; FD = Fibrotic dysplasia; ABC = Aneurysmatic bone cyst

Among the nine patients staged as B3, five did not relapse (two with giant cell tumors and three with aneurysmatic bone cysts). Four of these underwent operations with wide surgery and one with marginal surgery. In addition, three underwent prosthetic substitution, one underwent bone grafting with slippage and another underwent marginal surgery plus cementation (Table 10).

A patient with pelvic aneurysmatic bone cyst (B3) who was treated with selective arterial embolization and radiotherapy presented secondary malignant transformation to fibrosarcoma, five years after the treatment. The two tumors that became malignant evolved to fibrosarcomas that were staged as II-B. This patient underwent reoperation with wide surgical margins, femoral endoprosthesis for giant cell tumor in the distal femur and pelvic resection for aneurysmatic bone cyst in the iliac wing. After this procedure, the patient was treated with chemotherapy, but presented pulmonary metastasis and progressed to death.

The patient with multicenter giant cell tumor, with four epiphyseal lesions in the same lower limb, and another patient who presented pulmonary metastasis due to giant cell tumor, underwent thoracotomy and were cured.

The most common late complications were: four cases of lower-limb shortening in three patients with aneurysmatic bone cyst and one with fibrotic dysplasia, which were related to angular deformity and involvement of the growth plate; five cases of arthrosis, of which one was related to angular deformity due to fibrotic dysplasia and four occurred after cementation due to giant cell tumors: in the knee (proximal tibia, two cases), in the subtalar (calcaneal tumor) and in the wrist (distal radius tumor). There was only one case of late deep infection, in enchondroma of the proximal tibia that had been operated with cementation, and it was necessary to remove the cement (Table 11).

Table 10 – Aggressive tumors (B3) that did not relapse

Name	Type	Gender	Age	Staging	Surgery
1.VCA	GCT	F	15	GoT ₂ Mo	Marginal knee (tibia) + bone cement
2. JRA	GCT	F	13	GoT ₂ M ₁	Wide + knee endoprosthesis + thoracotomy
3. AJOR	ABC	M	30	GoT ₂ Mo	Wide + knee endoprosthesis
4. CAMS	ABC	M	29	GoT ₂ Mo	Wide + total hip prosthesis
5. EFA	ABC	M	17	GoT ₂ Mo	Wide + ankle bone graft and slippage (tibia)

Source: SAME HGIP, HO, HBH, HSF, 2008.

Table 11 – Complications

	Number of cases
Late arthrosis	5
Difference between limbs	4
Malignant transformation	2
Joint limitation	2
Varus deformity	2
Superficial infection	2
Femoral fracture	2
Genu valgum	1
Tendon rupture	1
Deep infection	1
Meralgia paresthetica	1
Hip bursitis	1

Source: SAME HGIP, HO, HBH, HSF, 2008.

DISCUSSION

The sample of this study was typical and was in agreement with the literature in all respects: most frequent tumors, age, sex and bones most affected^(7,8). The minimum follow-up for inclusion in the study was three years, because these lesions generally present relapse within the first two years after treatment⁽⁹⁻¹¹⁾.

Lesions in the active stage (B2) predominated, and simple bone cysts were diagnosed most frequently, by means of fractures. Clinical practice shows that most lesions that require medical attention, since they are symptomatic and cause fractures, are active benign lesions⁽¹²⁾.

It was also noted that the chances of failure of the surgical treatment, with consequent tumor relapse, increased through evolving from the latent stage (B1) to the active stage (B2) and progressively to the aggressive stage (B3), with statistical significance ($p < 0.001$) (Table 8). This study showed that bone cement (PMMA) was an effective adjuvant when associated with marginal surgery (Table 6). For the patients with giant cell tumors operated with cementation, the relapse rate was high, but similar to the findings of other published authors^(9,13,14). Greater reoccurrence among tumors staged as B3 is in agreement with some authors^(9,15), although others did not find a similar result^(10,16).

This study suggests that surgery with wide margins for aggressive (B3) benign lesions could control the lesion better, since it did not leave residual microscopic

disease and presented a lower relapse rate. However, because of the small sample at this stage, this information was not statistically significant ($p > 0.001$) (Tables 9 and 10). This affirmation is in agreement with the literature, in which it is reported that surgery, initially with wide margins, could reduce the risk of relapses, but at the cost of loss of function. For this reason, surgery with wide margins is not the preferred method and the risk of possible relapses is accepted^(6,8,17).

Apart from the two patients who evolved to malignant tumors and another patient who was lost from the follow-up, all the patients staged as B3 were cured, thus suggesting that the treatment was effective.

The absence of relapses in cases of latent tumors (B1) and the low rate of relapses for active lesions (B2) attest to the efficacy of expectant treatment and excision with or without autogenous iliac bone graft. This is corroborated by the literature^(7,8).

An analysis on the eight patients who presented relapses showed that the two patients whose tumors became malignant probably would not have been brought under control by any kind of treatment, since these cases were of high-grade fibrosarcoma (II-B)⁽¹⁻⁵⁾. One patient with giant cell tumor (B3) of the distal radius, who was lost from the follow-up could have been controlled with wide surgery and replacement with a fibular graft, as shown in the literature^(7,8), although there have been reports that giant cell tumors of the distal radius are more aggressive^(9,10). Four patients were cured by means of intracapsular reoperation with autogenous bone grafts. One patient with giant cell tumor (B3) of the proximal humerus was cured with wide surgery and replacement with an endoprosthesis (Table 9).

Complications such as primary malignant transformation and secondary transformation on radiotherapy^(18,19), pulmonary metastasis due to giant cell tumors⁽²⁰⁾ and multicenter presentation of giant cell tumors⁽²¹⁾ are well described in the literature. Post-cementation late arthrosis was not found by some authors^(10,15,22), but has been described by others, who have suggested using subchondral bone grafts to protect the cartilage⁽²²⁾.

The Enneking staging system is a surgical staging system that was created to serve as a guide for surgical treatment of musculoskeletal tumors. It was tested and adopted in 1980 by the Musculoskeletal Tumor Society (MSTS)^(1,2) and by the American Joint Committee for Cancer Staging and End Results Reporting (AJCC)⁽²³⁾.

The system was created at a time when simple radiographs were the only imaging examination used to stage patients. Up until now, this staging system has not been modified. It has remained unaltered for more than 25 years, over a period with great advances in imaging methods, genetics, molecular oncology, adjuvant therapy, bone grafting and surgical techniques⁽²⁴⁾.

From surveying the available literature, it can be seen that this staging system has not been statistically validated through broad-based multicenter studies. In 2002, the AJCC, which was using the Enneking system, made modifications to the staging of sarcomas, by replacing the compartmental location by the size of the tumor and dividing the patients into three categories: skip metastasis, pulmonary metastasis and other metastasis^(25,26).

The results from the present study confirmed that the Enneking staging system was very effective in de-

termining the prognosis, planning the surgery and indicating the adjuvant therapy for benign bone tumors and tumor-like bone lesions (Tables 6 and 7). This is the only system for benign bone lesions that exists and, to our knowledge through reviewing the literature, no studies on its validation have been published.

Although this study had the objective of evaluating the system and has proven its efficacy so far, we suggest that multi-institution studies, with samples including a greater number of patients, should be carried out in order to reevaluate the system and, possibly, to modernize it in the light of new knowledge.

CONCLUSION

The Enneking staging system was very effective in determining the prognosis, planning the surgery and indicating adjuvant therapy for benign bone tumors and tumor-like bone lesions.

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