Falling can be a Serious Problem for the Elderly

Likit Rugpolmuang, M.D.*, Charuwan Akewanlop, M.D., Suchart Benjarassamerote, M.D.***, Pornchai O-chareanrat, M.D.****, Pavanee Mahasitiwat, M.D.*****, Apichat Asavamongkolkul, M.D.***

**Department of Orthopaedics, **Department of Medicine, ***Department of Pathology, ****Department of Surgery, *****Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.*

ABSTRACT

We present the role of a multidisciplinary approach for the patient with a pathological fracture of the femur. A 56-year-old female complained of pain in the right hip from falling at home. After that she was sent for treatment without knowing her breast mass. For final diagnosis and treatment, the case was brought for discussion and made an appropriate treatment was made for her by the members of tumor board. With a multidisciplinary approach we saved not only her life but also the function of her leg.

Keywords: Metastatic breast cancer; Multidisciplinary approach; Pathological fracture

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The goals of treatment for patients with metastatic bone disease are to support, to control pain and to maximize their function. Supportive care is emphasised in both physical and psychological issues to provide the best quality of care to the patients. Nowadays metastatic bone tumors are common because people have a longer life expectancy than previously. The carcinomas that commonly occur in the elderly may be found with metastasis and can cause bone pain or even fracture. Whether the patient has a curable carcinoma or not, multidisciplinary approach is still the best way to treat the patient with these conditions. Sometimes even the psychological support has a role as a supporting system for the patients to adapt their life for the time they have left. When metastatic bone disease has occurred in someone, the patient who has the disease will try their best to get the best treatment for curing the disease. Sometime the disease cannot be cured but we think that we can give them the best practice in our country. A multidisciplinary approach is the only way to achieve all the goals the patients want, and not just in orthopaedic ways.

CASE REPORT

A 56-year-old Thai woman complained of pain in her right hip after falling for 10 days. She could not stand and walk independently due to the pain. She had no fever and nor history of weight loss. She had myasthenia gravis for 6 years and was treated with thymectomy. After the thymectomy and 1 year of medical treatment, she had no symptom. She was been regularly treated for hypertension and blood pressure which was well controlled. The personal and family history was negative for malignancy. The patient denied any history of drug allergy or use of addictive agents. She was not aware of her breast lump over her right chest wall. She had menopause for 7 years.

The physical examination at presentation revealed the patient was lying in the bed and could not move her right leg which had varus deformity and shortening of 1 cm. All the right neurovascular structures were normal. Her right breast had a mass of 4 cm in diameter at the lower and inner portions. The mass was movable without trill or ulcer. There was no lymphadenopathy along her neck and axillar areas.

Haematologic investigation revealed: Hct 35% (normal 37-52), RBC count 4.2* 10^6/micro litre, WBC 6.5*10^3/cubic mm (normal 4,000-11,000), plt 387,000 (normal 150,000-440,000), N 82%, L 12%. Urinalysis was within normal limit; blood chemistry showed the following: glucose 92 mg/dl (normal 76-110), BUN 16 mg/dl (normal 7-20), Cr 0.7 mg/dl (normal 0.5-105), ALK 457 U/l (normal 39-117); total calcium 10.5 mg/dl (normal 8.1-10.4); tumor markers: CEA 21.55 ng/ml (normal 0-3.4); AFP 5.60 IU/ml (normal 0-5.8); CA 19-9 (normal 0-39)9.68 U/ml; CA 125 20.51 (normal 0-35)U/m.

Radiographic Findings

Radiographic examination in the patient consisted of radiography of the right thigh. (Fig 1) The film showed an osteolytic lesion at the proximal femur beginning at the neck down to the subtrochanteric area. The lesion

Correspondence to: Likit Rugpolmuang
E-mail: likit105@yahoo.com

Fig 1. An AP radiograph of the right hip shows an osteolytic lesion at the subtrochanteric area with a pathological fracture.

extended from the cortex on the lateral side to the medial side which also causes thinning of the cortex. The proximal femur was aligned in the varus position with shortening of the subtrochanteric area. A bone scan revealed an area of increased radioactivity at the intertrochanteric region of the right femur, the posterior portion of the left 10^{th} rib, T7-8, T11-12, L5 spine and the right illiac bone. The conclusion of the bone scan was multiple bone metastasis.

Pathologic Findings

A submitted needle biopsy from the right breast demonstrated cancer cells arranged in ductal structures and showing hyperchromatic nuclei with striking abnormal mitosis. The cancer cells infiltrated around the breast tissue. It was diagnosed as invasive ductal carcinoma, moderately differentiated. Immunohistochemistry was performed and showed 80 percent positive staining with antibody against estrogen and progesterone receptors, while Her-2-neu was negative. These results confirmed that the patient had breast cancer (invasive ductal carcinoma). The tissue from the right proximal femur revealed multiple small irregular pieces of soft friable red-brown tissue which measured 3*2.5*1.2 cm in dimension. All the specimens were embedded for histological sectioning. Microscopic sections revealed small foci of typical epithelial cells showing a duct- like structure of tumor cells which showed an increased nuclear-cytoplasmic ratio, hyperchormatic nuclei and the loss of cell polarity. (Fig 2) Immunohistological staining performed on these tumor cells demonstrated the expression of estrogen and progesterone receptors which supported the diagnosis of metastatic breast cancer.

Diagnosis

We diagnosed bony metastatis of the breast cancer to the right proximal femur with pathological fracture.

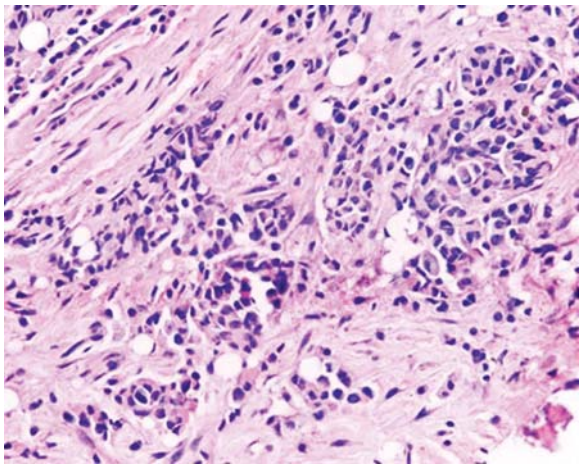

Fig 2. A Histological picture of the lesion at the Rt. thigh shows the atypical epithelial cells with a duct-like structure. The tumor cells show an increases nuclear- cytoplasmic ratio, hyperchromatic nuclei and loss of cell polarity.

DISCUSSION

A core needle biopsy was performed on the breast mass in order to find out the correlation of the disease with the proximal femur. Nevertheless the lesion at the proximal femur had to be treated surgically because it caused fracture. The fracture, which in the abnormal bone, is a pathological fracture, had to be treated by stable fixation in order for the patient to use the limb as normal for the rest of her life without pain. However the medical conditions had to be checked before the operation, especially the electrolyte imbalance, hypercalcemia which are commonly found in patients with metastatic bone disease. In patients who the serum calcium level has increased above 12 mg/ dl and who have the symptoms like nausea, vomiting, nocturia, fatigue and abdominal pain, their condition can be life threatening[1] and they need resuscitation to reduce the calcium level. For the treatment of pathological lesion we use the guidelines by Mirel; Mirel's score classification,[2] which is the interpretation from patient characteristics, size and location of the lesion to decide whether to perform prophylactic stabilization of the bone or not. If Mirel score is above 8, prophylactic stabilization of the bone to prevent fracture should be considered. But in this patient, we had already diagnosed the pathological fracture and she needed stabilization. Another advantage of surgical treatment is to take the tissue for pathological examination in order to get the staging and diagnosis of the disease.

To select the type of fixation in this kind of fracture, the information from the X-ray and bone scan must be evaluated preoperatively to locate the extent of the disease. If the disease extends along the whole femur surgical treatment has increased risk. The risks include massive bleeding, tumor emboli and prolonged operation, causing deterioration of the patient's condition and even death. It is very important to have intensive care nursing after the operation. Appropriate implants for fixation depend on the extent of the disease. If the femoral head and neck are involved we should also use an implant that can replace the diseases portion, such as hemparthroplasty[1]. But if the disease is limited to the proximal femur, as in this patient, intramedullary nailing is the proper procedure

over the side-plating. (Fig 3) Because of the mechanical advantage in load sharing and the proximity of the axis of the transmitting load for the intramedullary nail,it is better to compare with the side plate.

By using the intramedullary nail the patient can walk and return to normal activity fast postoperatively.

Management of a Palpable Breast Mass

When a mass or asymmetry is found in a clinical breast examination (CBE), the initial clinical approach is dependent on the ovulatory and menopausal status of the patient. Clinical examination of the breast can detect a mass, but it is not useful to distinguish a benign from a malignant process. Although there are some characteristics of breast cancer that may distinguish itself from a benign breast mass (e.g., indistinct borders, skin dimpling or nipple retraction), these however cannot reliably differentiate a malignant tumor from a benign mass. A comprehensive history, including age, menstrual status, parity, previous history of breast-feeding, family medical history, and drug usage should be noted. It is important to realize that there is nothing in the clinical history or risk-factor profile that can rule breast cancer in or out. Likewise, CBE can confirm breast masses but is notoriously inaccurate in definitively distinguishing their etiology, even among the most experienced examiners.

It cannot be overemphasized that any postmenopausal woman not on hormone replacement who presents with a breast mass should be assumed to have cancer until proven otherwise, since 85 percent of breast masses in women of 55 years and older are found to be cancerous. Among women on HRT, some have reversal of their breast tissue to a premenopausal state' that is, the tissue becomes more dense and prone to fibrocystic changes. A palpable breast mass in a postmenopausal woman on HRT has a highly unpredictable etiology.

The extent of imaging required evaluation of a solid breast mass depends on the age and risk status of the patient and the degree of clinical suspicion. Imaging studies are used to define the extent of a potential malignancy and to identify non-palpable masses elsewhere in the breast, findings that may influence the choice of local therapy. In women who are more than 40 years of age, diagnostic mammography is a standard part of the evaluation of a solid breast mass. In a patient with a breast complaint, a screening study consisting of two standard views of the breast (craniocaudal and mediolateral oblique) is inappropriate. The radiologist should be notified of the area of clinical concern so that it can be defined with a radio-opaque marker to ensure that any noted mammographic abnormalities correspond to the clinical finding. Extra views can be obtained to ensure that the lesion is adequately visualized. The purpose of this evaluation is to document the extent of the mass and the presence of other lesions within the breast that might influence the patient's suitability for breast-conserving surgery if cancer is diagnosed. Significant mammographic findings consist of alterations in density of breast tissue, calcifications, thickening of the skin, fibrous streaks, and nipple discharge. However, mammography alone may not be sufficient to rule out malignant pathology.

Fig 3. An AP radiographic picture of the pelvis demonstrates postoperative stabilization with a trochanteric nail.

Ultrasonography or magnified mammographic imaging of the breast containing the mass may provide additional information and may identify cysts or variations in normal breast architecture that is accounted for the palpable abnormality. Sonograms are most helpful when a mass cannot be felt, when the patient does not permit aspiration, or when a mass is too small and deep to offer a reliable target for aspiration. The combination of physical examination, mammography, and fine needle aspiration is highly accurate when all the tests give the same result.

Fine needle aspiration and cytologic examination have been shown to be efficacious, cost-effective, and highly reliable when cytologic preparation and cellular sampling are properly done. Aspiration is also effective for differentiating a cyst from a solid mass. If the fine needle aspiration cannot rule out cancer of the breast, a tissue biopsy (core cutting, needle biopsy or excisional biopsy) should be performed.

To lower the risk of missing a cancerous mass in the absence of an open biopsy, the principles of "triple diagnosis" are recommended. (Fig 4) "Triple diagnosis" refers to the application of 3 simultaneous steps in evaluating a breast mass: clinical assessment by palpation, mammography and FNAB. More recently, diagnostic ultrasound has been added to the equation. If the mass is "suspicious" by any of these methods, open biopsy is warranted.

Combining the results of CBE, radiologic imaging, and FNAB to evaluate a breast mass dramatically increases diagnostic accuracy. If the mass is interpreted as benign by all the 3 methods, the accuracy approaches 99 percent. A patient may then be given the facts to facilitate her choice between biopsy and follow-up. If follow-up is chosen, the authors recommend a first follow-up visit at 3 months after presentation and 3- to 6-month follow-up visits thereafter. Follow-up may be discontinued if the mass is stable for at least 1 year or if the mass resolves. Using this technique, the risk of missing a cancer diagnosis on the first evaluation is reduced to 1 percent.

Role of radiation therapy

The purposes of palliative radiotherapy in patients with bone metastases are to relief symptoms (bone pain), to improve the quality of the patient's remaining life (prevent further destruction, fracture and treat spinal cord compression) and postoperative radiotherapy to reduce the risk of progressive disease.[3]

Factors which should be considered before treatment are the clinical history (disease, previous treatment, pathology), physical examination and life expectancy. Patients who have received previous chemotherapy should

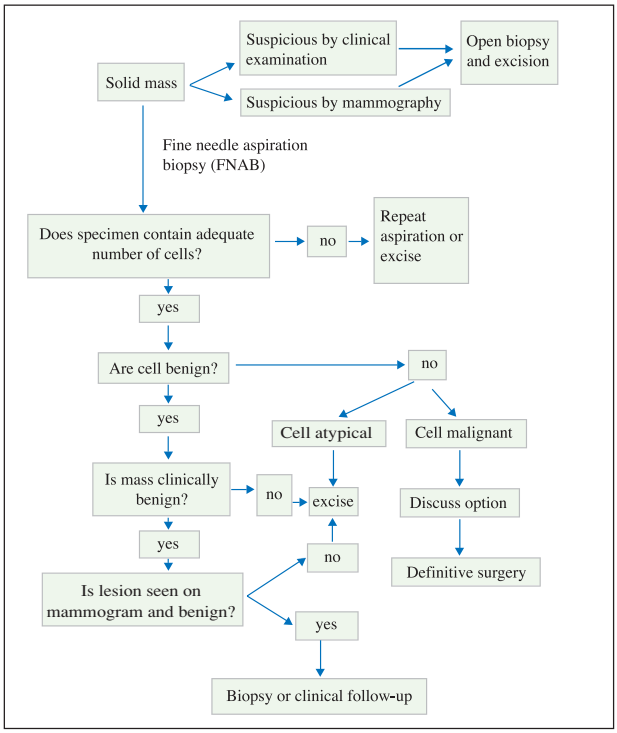

Fig 4. The algorithm of management of a palpable breast mass.

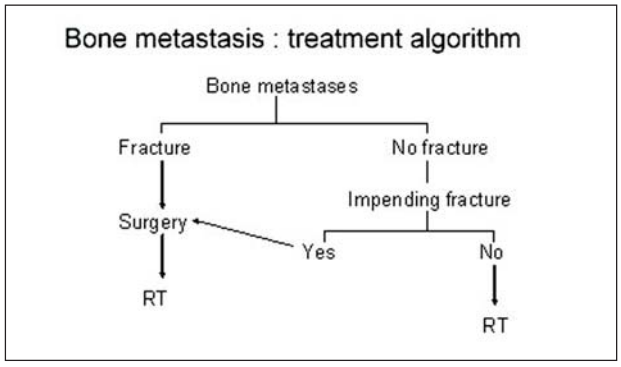

Fig 5. The flow chart of management of bone metastasis.

be checked for any bone marrow suppression and any previous doses of radiation should be taken into consideration before any re-irradiation in the same targeted area. The response to radiotherapy in hematological malignancy is better than in sarcoma. The patients with a short life expectancy and/or poor performance status should receive a shorter radiation course.

The dominant symptom of bone metastases (~75 percent) is pain, the characteristic pains are resting pain, progressive pain and night pain. About twenty-five percent of patients have no symptoms. The common primary sites of cancer (80 percent) are breast, prostate gland, thyroid gland, kidney and lung. The common locations of bone metastases are the vertebra, pelvis, ribs, proximal femur, humerus, scapula, sternum and skull.

Pathologic fractures occur in 8-30 percent of patients with bone metastases[4-6]. Proximal long bones are involved more commonly than distal bones. Consequently, pathologic fractures occur 50 percent of the time in the femur and 15% of the time in the humerus. The femoral neck and head are the most frequent locations for pathologic fracture because of the propensity for metastases to involve proximal bones and the stress of weight placed on this part of the femur. The four primary histologies that account for 80 percent of pathologic fractures include breast carcinoma (50-60 percent), kidney (10 percent), lung carcinoma (10 percent), and thyroid carcinoma (5 percent).

There are several imaging techniques for detecting bone metastases. A bone scan is a high sensitivity technique for screening for entire detection. Plain film x-ray shows fracture, impending fracture, osteolytic and/or osteoblastic lesions but is of lower sensitivity. A CT scan demonstrated differentiation between metastases and degenerative change and soft tissue involvement. The MRI study is an investigation of choice when the spinal cord or nerve root compression is suspected. The soft tissue involvement and the differentiation between benign and malignant vertebral collapse are also demonstrated by MRI. The treatment algorithm in patients with bone metastases is demonstrated as picture. (Fig 5)

The first evaluation is the fracture of the bone. If the patients have impending fracture and/or fracture, the appropriate treatment is surgery. Postoperative radiotherapy must be considered. The patients should receive radiotherapy to prevent further fracture if they have symptoms or the location of bone metastasis is at a weight bearing place or in the cervical vertebra.

The radiotherapies are composed of external radiotherapy (local and wide-field radiotherapy) and systemic therapy. The principles of local external radiotherapy are a small total dose (~8-30 Gy, 2/3 of curative dose), short course (1-2 weeks), small field and simple technique. Bone metastases are generally treated with shorter radiation courses that deliver lower total doses but with higher dose with each treatment. The common radiation schedules of local external radiotherapy are 30 Gy at 3 Gy per fraction, 20 Gy at 4 Gy per fraction and a single fraction of 8 Gy.

The RTOG conducted a prospective trial (RTOG 7402) that included a variety of treatment schedules which concluded that low dose, short-course treatment schedules were as effective as high dose, protracted treatment programs. Fifty percent of patients obtained relief of symptoms at 2-4 weeks after radiotherapy. The peak benefit was about 12-20 weeks after radiation. The median duration of pain control was 12 weeks. In the reanalysis, the number of fractions of radiotherapy used was statistically significantly correlated with re-treatment given, complete pain relief before treatment, and complete relief by combined pain and narcotic score, suggesting that the protracted course of treatment was associated with an improved outcome. The 8 Gy could be considered as probably "the lowest" optional single fraction on radiotherapy in the treatment of painful bone metastases.

In a meta-analysis of randomized trials comparing single-fraction radiotherapy regimens with multifraction regimens for palliation of metastatic bone pain, it was found that both regimens resulted in equivalent levels of pain relief but in different rates of re-treatment and pathologic fractures between arms. The RTOG 9714 demonstrated equivalence in terms of pain and narcotic relief at 3 months between 8 Gy delivered in a single treatment fraction and 30 Gy delivered in 10 treatment fractions over 2 weeks. The 8-Gy arm had a higher rate of re-treatment but had less acute toxicity than 30-Gy arm.

Wide-field radiotherapy or half body radiotherapy should be considered in patients who have multiple painful lesions, age 75 years, KPS 70, life expectancy

6 weeks and adequate bone marrow, renal and hepatic function.

The systemic therapy of radiotherapy is unseal source or radionuclide therapy (strontium 89 or summarium 153). This treatment should be considered in patients with multiple metastases, no evidence of spinal cord compression, pathological fracture, bone instability, good bone marrow reserve, need to avoid the complication of external radiotherapy and without a predominant painful site.

The patients who presented to us, received postoperative local external radiotherapy at the right hip and femur 30 Gy at 3 Gy per fraction.

Systemic Treatment of Metastatic Breast Cancer

Patients with metastatic breast cancer have great variability in their clinical courses. The median survival for these patients is in the range of 2 to 3 years. Prognostic factors associated with an indolent clinical course are: a long disease-free interval (usually at least 2 years from initial diagnosis), tumor with hormone receptor positivity, patients with response to prior therapy, lack of visceral involvement, limited sites of metastasis and a tumor with HER-2/neu negativity.

The primary goal in the treatment of patients with metastatic breast cancer is not curative. The treatment can prolong survival and improve quality of life. Therefore, treatments associated with minimal toxicity are preferred. The use of minimally toxic endocrine therapy is preferred to the use of cytotoxic therapy whenever reasonable. Patients considered to be appropriate candidates for initial endocrine therapy include those whose tumors are estrogen- or progesterone-receptor positive, those with bone or soft tissue disease only, and those with limited or asymptomatic visceral disease.

Systemic treatment for metastatic breast cancer:

1. Endocrine therapy: details are discussed below.
2. Chemotherapy:

There are several active chemotherapeutic agents used in the treatment of breast cancer: cyclophospamide / methotrexate / 5-FU (CMF), anthracyclines, taxanes, capecitabine, gemcitabine and vinorelbine.

3. Molecular-targeted therapy:

Trastuzumab is indicated for patients with metastatic breast cancers that over-express HER-2/neu.[7]

Endocrine therapy for metastatic breast cancer

- **Selective Estrogen Receptor Modulators (SERMs):** tamoxifen, toremifene. Tamoxifen is considered first-line therapy for patients with hormone receptor-positive, metastatic breast cancer.

- **Aromatase Inhibitors (AIs):** anastrozole, letrozole, exemestane. AI is indicated only in postmenopausal women. Recent evidence supports the use of AI as first-line therapy for patients with previous tamoxifen treatment.[8,9] As for postmenopausal women who have never received tamoxifen, AIs appear to have a superior outcome when compared to tamoxifen,[10] although the difference is modest. Therefore, either tamoxifen or an AI is an appropriate option in this setting.

- **Progestins:** megestrol acetate, medroxyprogesterone acetate. This group is considered to be used in second- or third-line therapy after failure of tamoxifen and/or AI.

- **Ovarian ablation** is indicated in premenopausal women as therapy for patients with previous tamoxifen treatment. It can be done by surgical oophorectomy or radiation therapy or using luteinizing hormone-releasing hormone agonist.

- **Bisphosphonates** (pamidronate or zolendronic acid) should be considered in patients with bone metastasis, especially if it is lytic, in addition to chemotherapy or endocrine therapy.

The patient presented with bone metastasis from breast cancer. She had no visceral metastasis. Based on the rationale discussed above, she received 20 mg /day of tamoxifen as a systemic treatment for her disease.

CONCLUSION

There are many modalities to provide the best treatment for the metastatic breast cancer. Depending on the doctors who pay attention for all modalities, sometime the alternative treatment that not mention here in the paper, has the role in the late stage of the disease. All physician should discuss with the patient for the modalities he offer and let them chose the best they want under supervision. The physicians should discuss with each others for managing the appropriate plan of treatment. So the patient will have the best plan then the good results are guarantee.

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บทคัดย่อ

กระดูกหักอันเกิดจากการแพร่กระจายของมะเร็งทุติยภูมิสามารถรักษาเพื่อยืดอายุผู้ป่วยและมีคุณภาพชีวิตที่ดีด้วยทีมสหสาขาวิชาชีพ

ลิขิต รักษ์พลเมือง พ.บ.*, จารุวรรณ เอกวัลลภ พ.บ., สุชาติ เบญจรัศมีโรจน์ พ.บ.***, พรชัย โอเจริญรัตน์ พ.บ.****, ภาวิณี มหาสิทธิวัฒน์ พ.บ.*****, อภิชาติ อัศวมงคลกุล พ.บ.***

**ภาควิชาศัลยศาสตร์ออร์โธปิดิคส์และกายภาพบำบัด, **ภาควิชาอายุรศาสตร์, ***ภาควิชาพยาธิวิทยา, ****ภาควิชาศัลยศาสตร์, *****ภาควิชารังสีวิทยา, คณะแพทยศาสตร์ศิริราชพยาบาล, มหาวิทยาลัยมหิดล, กทม 10700, ประเทศไทย.*

รายงานผู้ป่วยหญิงไทย อายุ 56 ปี ได้รับอุบัติเหตุลื่นล้มไม่สามารถลุกเดินได้ คณะผู้รายงานได้ทราบถึงปัญหาของกระดูกหักที่มีพยาธิสภาพอื่นอยู่ด้วย นอกเหนือจากภาวะกระดูกหักที่พบในผู้ป่วยทั่วไป จึงได้ปรึกษาและให้การรักษาโดยทีมแพทย์สหสาขา เพื่อให้การวินิจฉัยและการรักษาที่เหมาะสมสำหรับผู้ป่วยรายนี้ นอกเหนือจากการรักษาเพื่อให้ผู้ป่วยไม่ต้องเจ็บปวดจากภาวะกระดูกหักแล้ว ยังต้องให้การรักษาถึงต้นเหตุของกระดูกหักรายนี้ด้วย โดยมีจุดมุ่งหมายเพื่อให้ผู้ป่วยมีคุณภาพชีวิตที่ดีในช่วงเวลาที่ยังมีชีวิตอยู่