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SUMMARY

Metastases are one of the most frequent cause of pain in patients with cancer. Secondary lesions of prostate, breast and lung cancers constitute 80% of all the bone metastases.

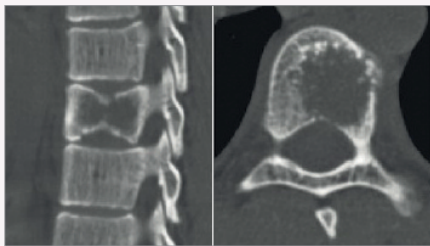
Commonly, cancer spreads to the bone via blood, but it can also be due to an invasion by contiguity from masses in adjacent soft tissues.

Most involved bone segments are the vertebrae. Percutaneous stabilization allows to reach safely and efficiently the main goal of palliative treatment of vertebral metastases.

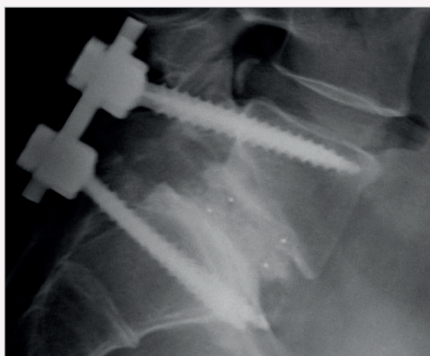
– This article aims to demonstrate how Osteobios™, as a support therapy, can be a valuable aid against osteoporosis, a condition that increasingly affects cancer patients.

KEY WORDS

CANCER, METASTASIS, OSTEOPOROSIS, PAIN, PERCUTANEOUS STABILIZATION, OSTEOBIOS™, QUALITY OF LIFE



http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1808-18512013000400016



https://en.wikipedia.org/wiki/Spinal_fusion

TREATMENT WITH OSTEOBIOS™ IN CANCER PATIENTS WHO UNDERWENT SPINAL STABILIZATION SURGERY THROUGH PERCUTANEOUS TECHNIQUE

INTRODUCTION

From an epidemiological point of view the three most frequent cancers (**lung**, **breast**, and **prostate**) are those that mostly cause skeletal metastases.

– The vertebral column is the skeletal segment most frequently affected. Symptomatic metastases of the rachis represent the clinical onset only in **30%** of patients with malignant neoplasia.

Vertebral bone involvement causes, over time, chronic pain subsequent to changes in posture, which derive, in turn, from the so-called “vertebral collapse”.

– The alterations of posture include, among others: large-scale kyphosis and abdominal protuberance with consequent respiratory deficit and/or abdominal symptoms (digestive difficulty, and constipation), as well as persistent forms of low back pain and sciatic neuralgia.

– The last decade has been character-

ized by substantial advances in the multidisciplinary diagnosis and in the management of patients with metastatic primary disease, and the resulting increase of patients’ survival and quality of life (QoL).

Most vertebral metastases are asymptomatic and do not require local treatment.

In a certain percentage of cases **pain** is the most common symptom; it is caused by the mechanical instability generated at the vertebral level.

Pain and limited ability to walk autonomously can affect importantly the QoL of these patients.

– Osteoporosis is a condition, mainly common in women after menopause, characterized by the reduction both quantitative and qualitative of the bone, which becomes more fragile and – therefore – more easily exposed to fractures.

The diagnosis of osteoporosis is obtained by conducting a low-dose radiation X-ray

exam, known as Bone Mineral Density (**BMD**) test. BMD test is expressed in terms of standard deviations (SD), in negative, from an average reference value typical of young/adult age (T score). Values inferior of 2.5 DS than this average (T score < -2.5) are typical of osteoporosis.

– This test, in conditions free of important risk factors, is indicated in women of age > 65; the BMD test before this age is recommended in women with menopause onset before 45 years, body weight inferior to 58 Kg, previous fractures given by bone fragility (individually or in other family members), tobacco addiction, and alcoholism.

In addition to the primitive forms of juvenile, senile and menopause osteoporosis, there are also forms secondary to diseases of the Endocrine System (hyperparathyroidism, Cushing's Syndrome, diabetes, hyperthyroidism), intestinal malabsorption (celiac disease), hemopathies (myeloma) and rheumopathies (rheumatoid arthritis and Systemic Lupus Erythematosus).

Even the lack of prolonged use of a limb or being forced to rest in bed are important risk factors for osteoporosis, as well as the prolonged use of certain drugs, such as cortisone-based drugs, anticoagulants, and thyroid hormones.

Osteoporosis can be controlled with an appropriate life-style: prevention in this sense should start before the age of 30, upon reaching the peak of bone mass, and is implemented in compliance with some dietary and behavioural rules which include adequate calcium intake with food (1,000 mg / day up to 50 years and up to 1,500 mg / day in women after menopause), daily exposure in the sunlight – which facilitates the synthesis of vitamin D, promoting the absorption of calcium present in foods (10-15 mins / day at least, up to 40 years and about 1h / day, 2-3 times / week, after 65 years), the regular practice of moderate physical activity, abolishing cigarettes and the limitation of alcohol and salt intake.

– It is to be remembered that calcium is present above all in milk and its derivatives; among these, in aged cheeses (e.g. Parmesan) in particular, in oily fish and in dried fruit (almonds, nuts, hazelnuts). Moreover, in the prevention of osteoporosis, the calcium taken with foods is more effective than the one administered via supplements, especially after 65 years.

– Among food supplements, **soy isoflavones** have proved useful to this purpose as they can facilitate the maintenance of bone density.

The earlier Low Dose Medicine is used, the more effective it is in individuals constitutionally more exposed to fractures.

– The goal of this therapy is to improve the QoL through a multifactorial treatment, consisting of analgesics, chemotherapy, radiotherapy, surgery and Physiologic Regulating Medicine (PRM).

Necessarily, the decision-making process regarding therapy has to consider the patient's life duration, the clinical symptoms, the general clinical condition, the amount of levels involved, age, the type of cancer, and the state of the previously irradiated area, if applicable.

Radiation therapy could be one of the standard treatment techniques for painful vertebral metastases, when no unstable fracture or imminent fracture are present.

In case of unstable fracture or imminent fracture, **spinal stabilization surgery** must be taken into consideration.

– In the last 10 years, minimally invasive stabilization techniques have been developed in spinal surgery to be applied not only in traumas, but also in degenerative diseases, and oncology.

– These **minimally invasive techniques** present potential advantages over open techniques, especially in that population of patients in whom surgery with palliative intent cannot and must not be considered.

The goals of surgery are mainly those of providing relief from pain, restore structural stability of rachis and prevent, reverse or improve neurological impairment, without causing excessive morbidity.

This technique is associated with minor soft tissue injuries and with an inferior incidence of post-operative infections and reduced blood loss.

– Minimally invasive stabilization also aspire to achieve results which are equivalent or higher than those of traditional open spinal surgery.

► This article presents a series of **16 cases** of metastatic spinal disease treated with minimally invasive stabilization, comparing the Performance Status (**PS**), the neurological functions, and the out-patient pre-operative and post-operative pain levels and status.

– Half of the patients were administered low dose therapy to prevent osteoporosis, which was present in all patients.

► The purpose was to verify if the minimally invasive technique with posterior access, associated or not with PRM therapy, could, in the short term, improve the pain control and the general clinical status.

MATERIALS AND METHODS

A consecutive series of **16 patients** (12 F and 4 M - average age 62.6 years) was selected. All patients had been undergoing surgery of percutaneous vertebral stabilization with minimally invasive technique for palliative purpose.

– Inclusion criteria were:

- metastasis in the vertebral column
- pain and/or vertebral instability
- previous surgically-treated vertebral collapse.

All patients were subjected to first- and second-level diagnostic procedures.

Pre-operative pain and QoL were carefully evaluated:

– pain was monitored using a subjective Numerical Rating Scale (NSR 0-10).

– QoL was assessed through neurological examination, walking ability and PS.

The PS was appointed a score from **0** to **3**, where **0** is equivalent to being able to carry out any activity as prior to illness; **1** to autonomous, able to ambulate, but not able to perform any activity; **2** to poorly sufficient, forced to rest in bed or sit for more than 50% of the time; **3** to nonautonomous, bedridden for almost all the time.

– All patients had undergone **spinal peduncle, minimally invasive percutaneous stabilization**.

During the follow-up, half of the patients (8) were administered a PRM medicine as prevention; the other half (8 patients) was administered a placebo, thus forming a Control Group.

The Active Group was administered **Osteobios™**, containing, among others: Bone 10, 30, 200X; Parathyroid gland

10, 30, 200X; Calcarea carbonica, fluorica, phosphorica 12, 30, 200X; Calcitonin 6X.

– This therapeutic option has been formulated for the following reasons:

- Parathyroid gland modulates the formation of osteoclasts (osteolytic action); such a modulation action is completed with the low dilution (6X) of Calcitonin, whose action, in addition to inhibiting osteoclast formation, favours the osteosynthesis.
- Low dilutions of Parathyroid gland are also considered effective in favouring the initial transformation of mesenchymal osteoprogenitor cells in osteoclasts. Without this transformation, osteoblasts (and thus osteosynthesis) cannot be obtained.

– The integrated action of the two low dose hormones ensures the restoration of the physiological balance, as above described.

RESULTS

The 16 patients suffered from metastases due to:

breast cancer (7), colon cancer (2), lung cancer (2), prostate cancer (2), melanoma (2), and kidney cancer (1) (TAB. 1).

The **1st level** analysis consists, in 8 cases, of a complete Nuclear Magnetic Resonance (NMR) of the vertebral column, in 5 cases of a Total-body Computed Tomography (TBCT) scan, in 2 cases of a Bone Scintigraphy, and in 1 case of a CT scan of the vertebral column only.

– The pre-operative evaluation was completed with a **2nd level** analysis including in 7 cases a CT scan of the vertebral column, in 5 cases a NMR, in 2 cases a Bone scintigraphy, in 1 case a Total-body CT scan, and in 1 case Total-body PET/CT scan (TAB. 2).

The bone segment more frequently involved was the **thoracic rachis** (7 cas-

TAB. 1

N.	Patient	Gender	Age	Primary cancer	Pre-operative NRS	Post-operative NRS	PS
1	AG	F	57	Breast	8	0	1
2	BA	F	47	Lung	8	0	0
3	CV	F	57	Breast	7	0	1
4	DF	M	62	Melanoma	6	1	1
5	DR	F	66	Lung	8	0	2
6	FP	M	66	Colon	6	0	1
7	GC	M	75	Prostate	7	1	2
8	IA	F	64	Breast	8	0	1
9	LR	F	45	Melanoma	6	3	1
10	ML	F	70	Colon	7	5	1
11	MA	F	83	Breast	10	3	2
12	MA	F	83	Breast	7	0	2
13	PN	F	57	Breast	10	5	1
14	PA	F	55	Kidney	5	0	0
15	SV	F	47	Breast	9	0	1
16	TA	M	68	Prostate	8	2	0

N.	Patient	Gender	Age	Primary cancer	1 st level analysis	2 nd level analysis
16	TA	M	68	Prostate	CT vertebral column	Bone scintigraphy
8	IA	F	64	Breast	NMR vertebral column	Bone scintigraphy
7	GC	M	75	Prostate	NMR vertebral column	PET/CT
1	AG	F	57	Breast	NMR vertebral column	CT vertebral column
13	PN	F	57	Breast	NMR vertebral column	CT vertebral column
15	SV	F	47	Breast	NMR vertebral column	CT vertebral column
6	FP	M	66	Colon	NMR vertebral column	CT vertebral column
14	PA	F	55	Kidney	NMR vertebral column	CT vertebral column
4	DF	M	62	Melanoma	NMR vertebral column	CT vertebral column
10	ML	F	70	Colon	Total-body CT	CT vertebral column
9	LR	F	45	Melanoma	Total-body CT	NMR vertebral column
3	CV	F	57	Breast	Total-body CT	NMR vertebral column
12	MA	F	83	Breast	Total-body CT	NMR vertebral column
2	BA	F	47	Lung	Total-body CT	NMR vertebral column
5	DR	F	66	Lung	Bone scintigraphy	NMR vertebral column
11	MA	F	83	Breast	Bone scintigraphy	Total-body CT

TAB. 2

es - 43.7%), followed by the **thoracic-lumbar** junction (6 cases - 37.5%), and the **lumbar segment** (3 cases - 18.7%).

Pre-operative pain assessment has not been registered in any patient as NRS < 5; 1 case scored 5; 3 cases scored 6; 4 cases scored 7; 5 cases scored 8; 1 case scored 9, and 2 cases scored 10.

Post-operative evaluation has shown an excellent improvement of the QoL with 9 patients who scored 0 (56.25%); 2 patients scored 1; 1 patient scored 2; 2 patients scored 3, and 2 patients scored 5.

No patient scored > 5; 75% of patients fall into the range 0-2. 4 patients reported the PS score equal to 2; 9 patients scored 1, and 3 scored 0 (TAB. 1).

The pre-operative ability to ambulate was limited in 3 patients and impossible in 1.

– After surgery all patients have achieved good recovery of the ambulation.

At pre-operative neurological assessment all patients reported lumbar pain, back pain or thoracic-lumbar pain, and 4 patients also presented walking disorders.

Post-operative neurologic assessment was negative in all cases (TAB. 3).

According to Tokuhashi and Tomita scores, the former indicated the simple palliation in 11 cases; the latter in 7 cases; no surgery in 5 cases.

– In all cases, optimal post-operative results were obtained both for pain and for walking ability.

All patients were subjected to post-operative CT scan on the day following surgery and they were quickly mobilized.

No wound dehiscence nor wound infection were reported.

► After 3 months, the 8 patients undergoing therapy with Osteobios™ underwent a Bone Mineral Density (BMD) test that highlighted not only the stabil-

ity of osteoporosis, but – in 3 patients – even a real improvement.

DISCUSSION

The continuous improvements in oncology have led to a significant increase in patients' survival.

30-40% of patients who develop vertebral metastases are burdened with a significant morbidity rate.

Lung cancer, breast cancer, and prostate cancer frequently metastasize to the vertebrae.

– The patients considered presented breast metastasis in 43.7% of cases, metastasis due to lung cancer, prostate cancer, colon cancer and melanoma in 12.5% of cases and metastasis due to kidney cancer in 6.3% of cases.

When dietary and behavioural prevention does not stop the disease, especially because of the above-mentioned risk

N.	Patient	Pre-operative deambulation	Post-operative deambulation	Pre-operative EON	Post-operative EON
1	AG	Yes	Yes	Dorsal pain	Negative
3	CV	Yes	Yes	Dorsal pain	Negative
4	DF	Yes	Yes	Dorsal pain	Negative
5	DR	Yes	Yes	Dorsal pain	Negative
8	IA	Yes	Yes	Dorsal pain	Negative
14	PA	Yes	Yes	Dorsal pain	Negative
15	SV	Yes	Yes	Dorsal pain	Negative
9	LR	Yes	Yes	Dorso-lumbar pain	Negative
12	MA	Yes	Yes	Dorso-lumbar pain	Negative
6	FP	Yes	Yes	Lumbar pain	Negative
10	ML	Yes	Yes	Lumbar pain	Negative
13	PN	Yes	Yes	Lumbar pain	Negative
2	BA	Limited	Yes	Lumbar pain + walking disorders	Negative
7	GC	Limited	Yes	Lumbar pain + walking disorders	Negative
16	TA	Limited	Yes	Lumbar pain + walking disorders	Negative
11	MA	No	Yes (with aid)	Lumbar pain + walking disorders	Negative

TAB. 3

factors, or pathologies that are associated with bone pathologies, the following can be administered:

- 1) drugs that oppose excessive bone resorption (bisphosphonates, estrogen, raloxifene);
- 2) drugs that stimulate neo-osteogenesis (parathyroid hormone derivatives).

The use of these drugs is often complicated by side effects.

– Regarding bisphosphonates, these include the problems related to their administration, even weekly, the irritative-harmful effect on the esophageal mucosa which forces to take them with empty stomach, standing, with plenty of water, and then fasting for about another half an hour.

The use of estrogen as hormone replacement therapy has been abandoned for the cardiovascular risks (my-

ocardial infarction and stroke for thromboembolic causes) and breast and ovarian cancers, the latter partially reduced with raloxifene, which acts in an anti-estrogen way on uterus and breast and in an anti-adsorbent way on the bones.

Finally, teriparatide, a synthetic component analogue to the parathyroid hormone, stimulating the bone formation; it is particularly expensive and indicated in daily injection therapy only for a period not > 2 years.

Also for this pathology, as for many others, are prescribed drugs whose risk / benefit ratio and manageability do not allow a prolonged use.

In many cases it is therefore advisable to opt for biological therapies which allow a higher compliance with those rules/behaviours favouring the prevention of several pathologies.

It is interesting to note that one of the risk factors of osteoporosis is the longitipical constitution.

These individuals present a certain fragility for genetic alterations in the skeletal formation, or impaired absorption of numerous trace elements, including calcium.

In these individuals a vicious circle occurs that, once started, is more and more difficult to control.

In such adults a further loss of calcium absorption is inevitable, for example during menopause, then causing a higher frequency in fractures.

About 70% of these patients have clinical evidence of vertebral disease only for pain, together with a reduced walking ability.

Also neurological impairment due to

the compression of the spinal cord or of the spinal nerve roots cause significant worsening of the QoL.

– It should also be considered that a vertebral collapse, when clinically manifest, causes pain and requires spinal stabilization, even if there is no spinal cord compression.

Metastatic lesions that affect the junctional segments produce more instability, vertebral collapse, pain and require stabilization of the vertebral column.

– Pain is the most common symptom which strongly influences the QoL of these patients.

Pain treatment is the first goal.

Percutaneous spinal stabilization with minimally invasive technique offers great support in the palliative treatment of patients with spinal metastases.

Vertebroplasty and kyphoplasty are procedures that can be performed even during the percutaneous insertion of screws.

These procedures, however, can produce serious complications in case of fracture of the posterior vertebral body or in case of vertebral collapse with leakage of cement or dislocation of the tumor in the vertebral canal.

In the pre-operative phase, after evaluating Tokuhashi and Tomita scores, we approved the palliative surgery also for the cases in which the surgery was motivated.

Surgical indication for vertebral metastatic lesions is being debated, considering on one side the surgical risks and on the other the patient's survival; surgery seems to play a palliative role, focusing on the patient's QoL.

Regarding the prognosis of these patients, the surgical risk must be moderated considering their life expectancy, their functional state and overall systemic condition.

Vertebroplasty and kyphoplasty by themselves are not enough.

– Percutaneous stabilization allows to achieve safely and effectively the main goal of the palliative treatment of vertebral metastases (i.e. relief from pain and stability of the vertebral column).

This procedure has not caused post-operative complications, which allowed to achieve the surgical goal in all cases.

The most frequent post-operative complication in these patients is given by wound infection (5-30% of cases).

Percutaneous stabilization has dramatically reduced this possibility.

– All patients were mobilized the day after the surgery and discharged the second or the third day.

– With PRM therapy, prevention can be started before the age of 30, with appropriate diet and physical activity. Nevertheless, there may be physiological conditions that prevent a correct absorption of the nutrients of many foods, or a skeletal and muscular structure inadequate to support physical efforts properly and for a long time.

Thanks to this sample of patients it has been possible to demonstrate how Osteobios™ represents a supportive therapy, a valid aid in the control of this pathology affecting more and more cancer patients. ■

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