Occurrence of malignant vertebral fractures in an emergency room setting

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Background: To perform a risk analysis study to determine the probability of a spinal fracture being of malignant origin in patients presenting at a level I trauma centre emergency room after trauma.
Patients and methods: Data from 334 consecutive patients were retrospectively obtained from 1993 to 2003. They were divided into two groups: group 1—(benign) traumatic fractures; and group 2—malignant fractures (n = 32). For statistical analysis independent Student t test, χ^2 test, and backward-stepwise logistic regression were used.
Results: The risk of vertebral fractures appearing to be of malignant origin increased with anatomical location (non-cervical—that is, thoracic or lumbar: odds ratio (OR) 48, 95% confidence interval (CI) 8 to 291), a history of malignancy (OR 72, 95% CI 12 to 422), trauma mechanism (that is, high energy: OR 0.03, 95% CI 0.003 to 0.28), and age >64 years (OR 3, 95% CI 0.9 to 12). Hence, patients over 64 years old attending the emergency room, with a vertebral fracture after a low energy trauma, had an approximately 50% chance of having a malignant fracture. With a non-cervical location and a history of malignancy this increased to 98%. Regardless of the trauma mechanism and age of the patient, a history of a malignancy and a non-cervical fracture posed at least a 36% risk of having a malignant fracture.
Conclusion: Supported by the present results we feel the probability of malignant fractures, although not frequently encountered, should always be considered in elderly and middle-aged patients with a history of malignancy and a non-cervical traumatic fracture.

Instigated by two earlier reports and a recent case at our clinic,[1 2] where a malignant C3 fracture presenting after minor trauma was not diagnosed as such at first presentation, we were interested in the occurrence of malignant vertebral fractures in the neurosurgical emergency room (ER) setting.

Differentiation between malignant and benign vertebral compression fractures is often problematic, even in non-traumatic fractures. This is particularly so in elderly patients and those receiving long-term steroid treatment who are predisposed to benign compression fractures caused by osteoporosis.[3 4] In addition to osteoporosis other causes of benign compression fracture include trauma or diseases such as haemangioma, eosinophilic granuloma, and Paget disease. Malignant compression fractures can be either metastatic or primary (bone tumours, multiple myeloma, malignant lymphoma, leukaemia).

Plain radiography and computed tomography (CT) scans are established imaging modalities in the evaluation of spinal fractures in the ER setting, but they are inadequate in differentiating the (compression) fracture's nature—that is, benign or malignant.[5–7] Establishing the correct diagnosis is of great importance in determining treatment and prognosis and, in case of reasonable doubt, additional magnetic resonance imaging (MRI) should be the imaging modality of choice.[8–10]

Advances in the treatment of tumours have improved the life expectancy of cancer patients appreciably, resulting in an increased incidence of metastatic skeletal disease (up to 75%) and increasing the risk of malignant fractures (up to 52% in breast cancer).[11] Since the incidence of malignant vertebral fractures presenting after trauma is not reported in the literature one could consider it under-reported. Nonetheless, it might be crucial for patient and disease prognosis to predict the a priori chance.

In the present study, we retrospectively collected data on all patients presenting at the neurosurgical ER with vertebral fractures. The occurrence of malignant fractures was studied and related to several patient characteristics. As far as we are aware, there are no previous reports in the literature regarding the prevalence of malignant fractures presenting after traumatic injury, except for a few case reports.[1 2] Therefore, we conducted a retrospective case–control risk analysis study.

PATIENTS AND METHODS

Ten year (1993–2003) clinical data from 334 consecutive patients attending the ER with a primary presentation of vertebral fractures after trauma were obtained retrospectively from the Erasmus Medical Center database. Demographic data such as age, gender, and a known history of malignancy were recorded. The latter was established through clinical records and patient/family anamnesis. Furthermore, the mechanism of injury and the Glasgow Coma Score (GCS) at admittance were registered. The site of the vertebral fractures—that is, cervical, thoracic, lumbosacral, or multiple sites—were retrospectively collected through plain *x* rays, CT and MRI scans when available.

Patients were divided into two groups: group 1—(benign) traumatic fractures; and group 2—malignant fractures diagnosed after trauma. Thirty-two patients (9.6%) were found to have malignant fractures. Follow up data were obtained through outpatient and clinical correspondence. The mean (SD) follow up period for both groups was: group 1, 4.9 (3.1) years; and group 2, 5.9 (3.6) years (p = 0.084). The cumulative patient follow up was 1472 and 189 years, respectively.

Abbreviations: B, mean regression coefficient; C3, third cervical vertebra; CI, confidence interval; CT, computed tomography; ER, emergency room; GCS, Glasgow Coma Score; MRI, magnetic resonance imaging; OR, odds ratio

Table 1 Patient characteristics

	Group 1 (n = 302)	Group 2 (n = 32)	p Value
Male/female	205/97	20/12	0.537
Age (year)	42.7 (20.3)	63.8 (12.4)	<0.001
GCS	13.7 (3.1)	15.0 (0.0)	0.019
Follow up (year)	4.9 (3.1)	5.9 (3.6)	0.084
Deceased	28 (9.3%)	5 (15.6%)	0.226

Group 1, traumatic fracture; Group 2, pathologic fracture.
All data are presented as mean (SD) unless otherwise indicated. The percentage between brackets is the percentage of patients within that group.
GCS, Glasgow Coma Score.

The diagnosis of a malignant fracture—that is, due to a metastasis of a previously known or unknown tumor—at the time of presentation in the ER after a traumatic event was confirmed by histopathology in 26 patients (81%). The six remaining patients were known to have and were treated before for primary tumors. Due to the clinical condition of these patients at the time of presentation (complete paresis, respiratory/cardiac instability) the diagnosis was made with additional radiological (CT, MRI) and nuclear imaging (bone scintigraphy).

For statistical analysis we used the SPSS10.0-package (SPSS, Chicago, Illinois, USA). To analyse differences between group 1 and 2, an independent Student t test and a χ^2 test was performed where appropriate. Data are presented as mean (SD). In order to perform a risk analysis all variables were dichotomised and initially univariately tested. Variables with $p>0.1$ were excluded from the final regression model. Backward stepwise logistic regression was used for this purpose and odds ratios (OR) and 95% confidence intervals (CI) are presented. For this, three age categories, using the calculated interquartile range of all 334 patients' ages, were proposed: age <33, age 33–64, and age >64 years. Furthermore, we calculated the average chance on a malignant fracture of individuals presenting at the ER with a vertebral fracture for the first time.

RESULTS

From a total of 334 successive spinal fractures, 32 (9.6%) were secondary to malignancy (group 2). Table 1 shows the characteristics of the patients in groups 1 and 2.

Although males were predominant in the population as a whole (67%), the gender distribution was equal between both groups. The age of patients with (benign) traumatic fractures (group 1) was significantly lower than that of patients of group 2: 42.7 (20.3) years vs 63.8 (12.4) years, respectively ($p<0.001$). The cause of the vertebral fracture in group 1 was a traffic accident (n = 134; 43.4%) or a fall (n = 104; 34.4%) in most cases. In group 2 there were 8 falls (25%), 1 traffic accident (3.1%), and minor trauma in 23 patients (71.9%). When arriving at the ER, patients in group 2 had a significantly higher mean GCS (group 1 vs group 2: 13.7 (3.1) vs 15.0 (0.0)). Thirty-one patients in group 1 had a GCS <8, compared to none in group 2 ($p = 0.056$). The medical history of the patients in group 1 showed freedom from disease in 177 cases (58.6%) and reported nine malignancies of any sort (3.0%); 21 patients (65.6%) in group 2 had a previous history of malignancy ($p<0.001$). In all of these, the vertebral metastasis originated from the known primary process. In the other 11 patients, the malignant fracture appeared to be the first manifestation of an unknown primary process at that time. During the follow up period, 28 patients (9.3%) in group 1 died, as compared to 5 (15.6%) in group 2 ($p = 0.23$).

Table 2 Vertebral fracture site

	Group 1 (n = 302) (%)	Group 2 (n = 32) (%)	p Value
Cervical	209 (69.2)	6 (18.8)	<0.001
Thoracic	44 (14.6)	17 (53.1)	<0.001
Lumbosacral	25 (8.3)	4 (12.5)	0.503
Multiple regions	24 (7.9)	5 (15.6)	0.177

Group 1, traumatic fracture; Group 2, pathologic fracture.
Shown are actual numbers. The number between brackets is the percentage of patients within that group.

The fracture site differed between both groups. A summary is presented in table 2. Vertebral fractures were mostly located at the cervical level (n = 209; 69.2%) in the case of a traumatic fracture (group 1), whereas malignant fractures more frequently involved the thoracic levels (group 1 vs group 2: 14.6% vs 53.1%, $p<0.001$). No differences were observed when fractures involved lumbosacral or multiple sites (table 2).

After dichotomisation and univariate analysis, the following variables were included into the logistic regression model: cervical spine fracture (yes/no), thoracic spine fracture (yes/no), GCS <8 (yes/no), history of malignancy (yes/no), trauma mechanism (low/high energy), age <33 years (yes/no), and age >64 years (yes/no). It appeared that a non-cervical fracture—that is, thoracic or lumbar (OR 47.6, 95% CI 7.8 to 291.2), a history of malignancy (OR 71.5, 95% CI 12.1 to 422.6), and a low energy trauma (OR 35.7, 95% CI 3.6 to 333.3) proposed the highest risk for a vertebral fracture at first presentation to be of malignant origin rather than traumatic. Additionally, an age of over 64 years also gave an increased risk (OR 3.3, 95% CI 0.9 to 12.2). Table 3 shows the last step of the logistic regression analysis.

From this, the chance of a malignant fracture in an individual presenting at the ER with a vertebral fracture for the first time could be calculated (table 4). Individual patients <64 years of age had an insignificant chance of a malignant vertebral fracture, whereas older patients, engaged in a low energy trauma, had at least a 50% chance, regardless of anatomical site or medical history. Regardless of the trauma mechanism and age of the patient, a history of a malignancy and a non-cervical fracture posed at least a 36% risk of having a malignant fracture. With a positive history of malignancy and a non-cervical—that is, thoracic or lumbar—fracture, the chance of a malignant fracture increased up to 95% and 99% for patients younger and older than 64 years, respectively.

DISCUSSION

In this study we have retrospectively determined clinical risk factors for vertebral fractures, presenting after trauma at the ER, appearing to be of a malignant nature. Odds ratios for non-cervical (thoracic and lumbar) fractures, a positive history of malignancies, trauma mechanism (high energy), and an age over 64 years were calculated (47.6, 71.5, 0.0 and 3.3, respectively) (table 3). It turned out that fractures at the thoracic and lumbar level carry a high risk of malignancy in patients of all ages with a previous history of malignancy (36–99%, dependent on mechanism of injury). Patients older than 64 years of age, engaged in a low energy trauma, had an overall 50% chance to have a malignant fracture. When a history of malignancy was apparent and the fracture was located as being either thoracic or lumbar, this chance increased up to 99% (table 4).

Three case reports in the English literature were found showing malignant fractures of the cervical spine as the initial presentation in an ER setting.[1 2] Chan *et al* stress the importance of considering malignant fractures in elderly patients presenting with neck pain or neurological symptoms following minor trauma, which corroborates our results regarding increased age

Table 3 Logistic regression model with variables influencing the risk on a pathologic vertebral fracture

	B (SE)	Wald	OR (95% CI)	p Value
Non-cervical fracture	3.9 (0.9)	17.5	47.6 (7.8 to 291.2)	<0.001
History of malignancy	4.3 (0.9)	22.2	71.5 (12.1 to 422.6)	<0.001
High energy trauma	−3.6 (1.2)	9.4	0.0 (0.0 to 0.3)	0.002
Age >64 years	1.2 (0.7)	3.1	3.3 (0.9 to 12.2)	0.081
Constant	−5.1 (1.0)	27.2	0.0	<0.001

B, mean regression coefficient; CI, confidence interval; OR, odds ratio; SE, standard error of the mean; Wald = $(B \cdot SE^{-1})^2$.

Table 4 Chance (%) of a pathologic vertebral fracture for different age categories

	Cervical fracture: no history of malignancy	Cervical fracture: history of malignancy	Non-cervical fracture: no history of malignancy	Non-cervical fracture: history of malignancy
Age ⩽64 years, high energy trauma	0.02	1.2	0.8	36.3
Age >64 years, high energy trauma	0.05	3.7	2.5	64.9
Age ⩽64 years, low energy trauma	0.6	30.2	22.4	95.4
Age >64 years, low energy trauma	1.9	58.5	48.4	98.5

The numbers represent chances (percentages).

and the greater chance on malignant fractures.[2] Furthermore, they state that malignant fractures involving the cervical spine are less common than fractures to the thoracic and lumbar spine. Indeed, the present study has shown that the presence of a non-cervical—that is, thoracic or lumbar—fracture raises the suspicion for malignancies.

Although 8% of patients present with spinal cord compression due to vertebral metastasis as the initial presentation of their primary malignancy,[12] there are few data on the prevalence of malignant fractures presenting at the ER after (minor) trauma. In our series the percentage of malignant fractures approached 10%, a significant number of patients. Due to the retrospective nature of the present study, this might even be an underestimation, because only histologically proven cases or cases with a high probability for a malignant fracture were included as such. Consequently, we believe that the emergency care giver should be prepared and provided with the appropriate diagnostic armamentarium to detect a possible underlying primary malignant or metastatic cause of vertebral fractures.

Vertebral fractures with no evident cause or fractures due to minor trauma are suspicious for malignant fractures, but they can also indicate (benign) osteoporotic fractures seen in the elderly or patients on steroid treatment.[3 4 13] In our series 71.9% of malignant fractures presented after minor trauma, indicating that further imaging and laboratory tests might be required when minor traumatic events lead to vertebral fractures. Since therapeutic options are available to relieve pain, neurologic symptoms or immobility, we believe that further diagnostic work-up is essential to establish the correct diagnosis.[14–16] In a recent article, Uetani and colleagues review the use of MRI in the differentiation between malignant and benign compression fractures. They conclude that by applying the constellation of morphological and signal intensity criteria this differentiation can be made correctly with a high degree of certainty.[9] Other authors also propagate the use of MRI to help diagnose malignant vertebral fractures.[8 17 18]

Taking into account the various drawbacks of a retrospective study and the lack of any prospective data, we feel that whenever the a priori chance of malignant vertebral fracture is high, additional imaging by the use of MRI should be performed to rule out malignancy. As a consequence of the presented data this would by all means imply patients with a positive history of malignancy and a thoracic or lumbar fracture site, regardless of their age.

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