ORIGINAl ARTICLE

Is preoperative embolization a prerequisite for spinal metastases surgical management?

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KEYWORDS
Spinal metastases; Embolization; Surgery; Risk of hemorrhage

Summary
Background: Preoperative embolization decreases the intraoperative risk of hemorrhage in spinal decompression surgery of hypervascular metastases such as renal cell carcinoma. There is no consensus concerning embolization in other metastases. The purpose of this study was to compare the intraoperative amount of blood loss in embolized versus non-embolized patients, seeking for differences depending on the primary tumor and the extent of surgery.

Patients and methods: Ninety-three patients, average age 60.5 years, were operated. The origins of metastases were: 28 breast cancer (30.1%), 19 pulmonary carcinoma (20.4%), 16 renal cell carcinoma (17.2%), 30 other cancers (32.3%). Surgical procedures were: 52 thoracolumbar laminectomies with instrumentation, 29 thoracolumbar corpectomies or vertebrectomies, 12 cervical corpectomies. A preoperative microsphere embolization was performed in 35 patients. Blood loss was evaluated by: blood volume in surgical aspiration devices, number of transfused packed red blood cells units and hemoglobin variation during surgery.

Results: Renal metastases were systematically embolized. In the breast group, there was no significant difference (P > 0.05) in blood loss between embolization versus non-embolization. In the pulmonary group and in other metastases, no difference was found either. The extent of surgery (corpectomy/vertebrectomy versus thoracolumbar instrumentation and cervical corpectomy) increased bleeding: breast 1775 ml versus 778 ml and 600 ml respectively (P = 0.048), pulmonary 2500 ml versus 430 ml and 180 ml (P = 0.020), renal 3346 ml versus 1175 ml and 780 ml (P = 0.036) and others 1550 ml versus 474 ml and 400 ml (P = 0.020).

Conclusions: Embolization decreases the risk of hemorrhage in highly vascularized metastases such as renal cell carcinoma. A benefit of embolization was not found for metastases of breast...
Introduction

Metastatic vertebral lesions can severely reduce the quality of life in terms of tumor-associated pain, pathologic fractures and the risk of paraplegia. Surgical stabilization and neural decompression belong to the standards of oncologic management of spinal metastases. However, certain metastatic lesions present an elevated risk of hemorrhage and transarterial embolization was found to be a valuable method of decreasing intraoperative bleeding [1–3].

Metastases of well-vascularized primary tumors, such as renal cell carcinoma, are frequently found in the spine. About 65 to 75% of these metastases are themselves hypervascularized [2,4]. Therefore, there is a risk of massive blood loss in renal cell carcinoma. When embolization is not performed, bleeding and technical difficulty may increase, which inhibits sufficient removal of metastatic tissue and augments the patient’s morbidity [5].

However, it remains unclear if it is useful to embolize metastases of other primary tumors such as hepatocellular carcinoma, germ cell tumors, and neuroendocrine tumors. Other hypervascular tumors such as thyroid carcinoma is still controversial [6,7] and melanoma do not seem to be amenable to embolization [8]. The possible effect of preoperative embolization in frequent metastases such as breast cancer or pulmonary carcinoma has not been published to our knowledge.

This retrospective study was conducted to compare the intraoperative amount of blood loss in embolized versus non-embolized patients who underwent surgical treatment of spinal metastases, seeking for differences depending on the primary tumor as well as the extent of the surgical procedure.

Patients and methods

Patients

Institutional review board approval was obtained for this retrospective study. A total of 93 consecutive patients with spinal metastasis were operated by three senior surgeons in our department between March 2000 and December 2009. The average age at operation was 60.5 (range 34–81) years. There were 51 male (54.8%) and 42 female (45.2%) patients. Patients were regularly followed up clinically and radiographically by their operating surgeon. Thirty out of 93 patients (32.3%) presented more than one metastatic vertebral level. A total of 132 levels were operated: 27 cervical, 76 thoracic and 29 lumbar. Forty-eight out of 93 patients (51.6%) had associated visceral metastases. Surgical indications were either curative in cases of single metastasis, or palliative if the metastasis infiltrated surrounding tissues, if several metastases or a pathologic fracture were present.

Types of primary tumors

Four main groups of different metastases origins were lined out in 93 patients: 28 breast (30.1%), 19 pulmonary (20.4%), 16 renal (17.2%) and 30 other tumors (32.3%).

The origins of other tumors was composed of: five colorectal, four prostate, three esophagus, three melanoma, three urothelial carcinoma, two thyroid, two pharynx, two uterus, one corticosurelanoma, one hepatocarcinoma, one chondrosarcoma, one Ewing sarcoma, one non-Hodgkin lymphoma and one neuroendocrine tumor.

Surgical procedures

Three different categories of surgical intervention were defined:

- posterior instrumentation of the thoracolumbar spine associated with a laminectomy and a partial tumorectomy if necessary;
- thoracolumbar corpectomy or vertebrectomy with an anterior cage implantation and a posterior instrumentation;
- cervical corpectomy using an anterior plate with either a cage or the iliac crest for the replacement of the vertebral body.

The respective numbers of patients in each of these categories were: 52 in group (1), 29 in group (2) and 12 in group (3).

Preoperative embolization

A preoperative embolization was performed in 35 out of 93 patients. In this retrospective cohort, except for one case, renal cell carcinoma was systematically embolized. The choice of embolization for other metastases types was based on two main criteria: preoperative magnetic resonance characteristics indicating hypervascularity by contrast media enhancement or in patients for whom radical surgery was planned. A superselective catheter technique was used to perform an angiography through a femoral approach first. Once the vascular bed of the tumor was identified, the embolization was realized using microspheres.
with a diameter ranging from 500 to 700 μm (Embosphere®, BioSphere Medical, Rockland, MA). The embolization was performed within 48 h prior to surgery to avoid the revascularization of the tumor. Selective catheterization of intercostal or lumbar segmental arteries was also used to check if there was a direct link between the Adamkiewicz artery and the tumor vascularization. This was the case in two patients, where the embolization was performed partially in order to preserve the blood supply to the anterior spinal artery.

Parameters describing blood loss

Three parameters were used to quantify the amount of blood loss during surgery and the immediate postoperative period:

- the intraoperative blood volume in the suction was measured in milliliters;
- the number of transfused packed red blood cell units until the fifth day after surgery;
- the hemoglobin variation from the beginning to the end of surgery was calculated in gram per deciliter, adjusted to the number of transfused packed red blood, using the formula: hemoglobin variation = (hemoglobin initial – hemoglobin final) + number of transfused packed red blood cell units. One packed red blood cell unit was considered to increase the hemoglobin rate by 1 g/dl.

Statistics

Statistical evaluation was performed with R statistical software version 2.10.1 (http://www.R-project.org). A quantitative evaluation has been performed for each type of metastasis prior to further statistical evaluation in different primary tumor subgroups. The effect of embolization on the amount of blood loss and the hemoglobin variation was evaluated for each type of primary tumor using a linear regression model adjusted on the type of surgery. A Poisson model was used to investigate the influence of embolization on the number of transfused packed red blood cells. The significance level was set at $P < 0.05$.

Results

Blood volume in suction during surgery

The analysis of intraoperative blood loss by quantifying the volume in the suction did not show significant differences between the tumor subgroups. However, the type of surgical procedure did significantly influence the amount of blood loss. Corpectomies and vertebrectomies increased the average volume of blood loss compared to thoracolumbar decompressions with instrumentation and cervical corpectomies (Table 1).

Number transfused packed red blood cell units

The same observation was made when considering the average number of transfused red blood cell units in the different tumor subgroups. Corpectomies and vertebrectomies increased the number of transfused red blood cell units compared to the group decompression with instrumentation and cervical corpectomy (Table 2).

Intraoperative hemoglobin decrease

The same observation was observed for the hemoglobin variation from the beginning to the end of surgery in different tumor subgroups. Corpectomies and vertebrectomies increased the hemoglobin difference compared to decompressions with instrumentation and cervical corpectomies (Table 3).

Influence of embolisation in different tumor subgroups

The numbers of embolized and non-embolized patients sorted by type of surgical intervention are demonstrated in Table 4 for each tumor subgroup.

In the breast cancer group, eight patients were embolized and 20 patients were operated without embolization. Six out of eight embolized patients underwent a vertebrectomy or a corpectomy. The linear regression model and the Poisson model adjusted on the type of surgery indicated that the blood loss was not significantly increased for non-embolized patients who received a thoracolumbar instrumentation and decompression or a cervical corpectomy for the different parameters: blood volume in suction ($P = 0.235$), number of transfused packed red blood cells units ($P = 0.404$), hemoglobin variation ($P = 0.754$). A case of single metastasis of L3 is illustrated in Fig. 1. This patient underwent embolization which occluded the tumor vascularisation (Fig. 2) prior to surgical treatment by vertebrectomy of L3 and posterior instrumentation from L2 to L5 (Fig. 3).

Table 1  Average blood volume in suction (ml) during surgery for each group of primary tumor and for each category of surgical procedure.

<table>
<thead>
<tr>
<th></th>
<th>Posterior instrumentation and decompression</th>
<th>Thoracolumbar corpectomy or vertebrectomy</th>
<th>Cervical corpectomy</th>
<th>P-value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>778</td>
<td>1775</td>
<td>600</td>
<td>0.048</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>480</td>
<td>2500</td>
<td>180</td>
<td>0.036</td>
</tr>
<tr>
<td>Renal</td>
<td>1175</td>
<td>3346</td>
<td>780</td>
<td>0.020</td>
</tr>
<tr>
<td>Others</td>
<td>474</td>
<td>1550</td>
<td>40</td>
<td>0.020</td>
</tr>
</tbody>
</table>

\(^a\) Comparison corpectomy or vertebrectomy versus instrumentation and decompression/cervical corpectomy.

Table 2  Average number transfused packed red blood cells units for each group of primary tumor and for each category of surgical procedure.

<table>
<thead>
<tr>
<th></th>
<th>Posterior instrumentation and decompression</th>
<th>Thoracolumbar corpectomy or vertebrectomy</th>
<th>Cervical corpectomy</th>
<th>P-value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>1.2</td>
<td>4.6</td>
<td>0</td>
<td>0.002</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>0.4</td>
<td>3.5</td>
<td>0</td>
<td>0.007</td>
</tr>
<tr>
<td>Renal</td>
<td>2.7</td>
<td>4.0</td>
<td>0</td>
<td>0.006</td>
</tr>
<tr>
<td>Others</td>
<td>0.4</td>
<td>2.8</td>
<td>0</td>
<td>0.001</td>
</tr>
</tbody>
</table>

\(^a\) Comparison corpectomy or vertebrectomy versus instrumentation and decompression/cervical corpectomy.

Table 3  Average intraoperative hemoglobin decrease (g/dl) for each group of primary tumor and for each category of surgical procedure.

<table>
<thead>
<tr>
<th></th>
<th>Posterior instrumentation and decompression</th>
<th>Thoracolumbar corpectomy or vertebrectomy</th>
<th>Cervical corpectomy</th>
<th>P-value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>3.6</td>
<td>8.0</td>
<td>2.7</td>
<td>0.090</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>2.8</td>
<td>7.1</td>
<td>2.9</td>
<td>0.260</td>
</tr>
<tr>
<td>Renal</td>
<td>4.4</td>
<td>7.9</td>
<td>3.3</td>
<td>0.078</td>
</tr>
<tr>
<td>Others</td>
<td>2.4</td>
<td>4.9</td>
<td>2.0</td>
<td>0.003</td>
</tr>
</tbody>
</table>

\(^a\) Comparison corpectomy or vertebrectomy versus instrumentation and decompression/cervical corpectomy.

Table 4  Number of embolized and non-embolized patients sorted by tumor subgroups and type of surgery.

<table>
<thead>
<tr>
<th></th>
<th>Instrumentation and decompression</th>
<th>Corpectomy or vertebrectomy</th>
<th>Cervical corpectomy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Embolized</td>
<td>Non-embolized</td>
<td>Embolized</td>
<td>Non-embolized</td>
</tr>
<tr>
<td>Breast</td>
<td>2</td>
<td>15</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>2</td>
<td>13</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Renal</td>
<td>6</td>
<td>1</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>10</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>39</td>
<td>21</td>
<td>8</td>
</tr>
</tbody>
</table>

In the group of pulmonary tumors, three patients were embolized and 16 patients were non-embolized. One out of three embolized patients underwent a vertebrectomy. The statistical models did not indicate a significant difference between embolized and non-embolized patients: blood volume in suction (P = 0.094), number of transfused packed red blood cells units (P = 0.273), hemoglobin variation (P = 0.960).

In the group of renal cell carcinoma, 15 out of 16 patients were embolized. The single patient who was not embolized presented with an acute paraplegia and underwent a thoracic instrumentation and decompression which led to a blood loss of 2000 ml. A statistical comparison between embolized and non-embolized patients could not be performed in this subgroup. The intraoperative blood loss varied from 100 to 8750 ml in patients who underwent preoperative embolization.

In the group of other tumors, nine patients underwent embolization and 21 patients were operated without embolization. One out of three embolized patients presented with an acute paraplegia and underwent a thoracic instrumentation and decompression which led to a blood loss of 2000 ml. A statistical comparison between embolized and non-embolized patients could not be performed in this subgroup. The intraoperative blood loss varied from 100 to 8750 ml in patients who underwent preoperative embolization.

underwent a vertebrectomy. A significant difference between embolized and non-embolized patients could not be lined out using statistical models: blood volume in suction ($P=0.994$), number of transfused packed red blood cells units ($P=0.691$), hemoglobin variation ($P=0.963$). In this group, the two patients with metastasis of thyroid carcinoma underwent a cervical corpectomy without preoperative embolization and had an intraoperative blood loss of 500 and 800 ml respectively.

Discussion

Transarterial embolization represents a useful method of decreasing intraoperative bleeding in certain metastatic lesions of the spine [1]. Historically, gelfoam particles were flushed through a catheter into the tumor vascular bed [9]. Other materials such as dura-isobutyl or polyvinyl alcohol (PVA) were also used [6]. The efficacy of coils in vertebral metastases remains controversial, since larger particles may occlude pretumoral arterial branches but without complete filling of the microvascular structures of the tumor [2,10]. Microspheres might be preferable to achieve a complete embolization and to further delay the revascularization of the tumor [11]. The use of PVA or gelatin sponge microparticles leads to a significant reduction of blood loss during surgery [3]. However, in some tumors such as renal cell carcinoma, the use of coils seems to be ineffective because of an angiomatous vascularity [12].
Several studies [2,3,8,13] have shown that embolization is particularly valuable in metastases of renal cell carcinoma which present an elevated risk of hemorrhage. Recently, Wilson et al. [14] have compared the risk of intraoperative bleeding in different tumor types and demonstrated that renal cell carcinoma was associated with a significantly higher risk of hemorrhage. Roscoe et al. [4] described catastrophic intraoperative hemorrhage during surgical stabilization of pathologic fractures due to renal cell carcinoma, which can lead to life threatening conditions for the patient. Olerud et al. [5] reported uncontrollable bleeding of 15000 ml in a patient who underwent a vertebrectomy and died four days after surgery. Manke et al. [12] reported a median blood loss of 1500 ml (300 to 8000 ml) in 17 embolized patients versus 5000 ml (1440 to 15000 ml) in 10 non-embolized patients. It is therefore current practice to perform a diagnostic spinal angiography followed by embolization when feasible in all patients with renal metastatic lesions to the spine in whom surgical resection is planned. Even partial embolization of renal cell metastatic lesions seems to reduce blood loss compared to non-embolized tumors [12]. However, in spite of favorable results in renal cell carcinoma, radical preoperative embolization is not always a guarantee of avoiding extreme blood loss during surgery [13,15]. This is concordant with our findings, which found an extremely variable blood loss between different patients ranging from 100 to 8750 ml despite embolization.

Metastases of follicular and papillary thyroid carcinoma are classified as hypervascular tumors and preoperative embolisation seems to be beneficial in reducing the amount of blood loss [1,2,16,17]. The arterial feeder vessels to these hypervascular tumors are usually large and accessible by superselective microcatheterization [6,7]. However, the number of patients in these studies remains relatively low. In our series, the two patients who underwent cervical corpectomy without embolization lost a blood volume of 500 and 800 ml respectively, which is contradictory with previous findings. Smit et al. [6] reported that embolisation of metastases of follicular thyroid carcinoma could effectively diminish the vascular supply of vertebral tumoral lesions and qualified this procedure as an attractive option when performing a surgical decompression in combination with irradiation and radioiodine therapy. Court et al. [7] reported on 18 patients with metastasis of thyroid carcinoma and recommend a systematic preoperative embolization.

Radeleff et al. [1] and Vetter et al. [16] reported on some patients who underwent preoperative embolization of spinal metastases of breast cancer and Guzman et al. [18] included one patient with metastasis of bronchial carcinoma in his series. However, a possible benefit of embolization was not described in these studies, compared to the positive effect noticed in renal cell carcinoma, thyroid carcinoma or hepatocellular carcinoma. In the present study, the mammary or pulmonary origins of spinal metastases did not seem to appear as predictive factors for increased intraoperative bleeding. Embolization does not seem to have a significant influence the average volume of blood loss. However, only eight patients were embolized in the breast cancer group and three patients in the pulmonary tumor group. Seven of these patients underwent thoracolumbar corpectomies or vertebrectomies. It remains difficult to properly analyze the real effect of embolization from this retrospective data. Rehak et al. [13] described a 2.7-time higher blood loss in embolized patients in comparison to non-embolized patients. This is probably due to the fact that a patient selection is performed by the surgeon preoperatively. This represents a bias in the evaluation of retrospective data which has to be considered in our study.

Major interventions such as thoracolumbar corpectomies or vertebrectomies increased the average volume of blood loss in any type of spinal metastasis which is related to the extent of the surgical technique. These indications should be restricted to single metastasis which are relatively rare compared to palliative procedures such as decompression and instrumentation in patients with multiple metastasis. Berkefeld et al. [10] described an average blood loss of 4350 ml in non-embolized patients who underwent a corpectomy versus 2650 ml in patients who received an embolization with coils, 1800 ml with PVA particles and 1850 ml with PVA particles and coils. Olerud et al. [5] reported an average blood loss of 6200 ml in non-embolized patients versus 4300 ml after embolization with gelfoam or PVA particles. Boudghene et al. [19] found an average blood loss of 5900 ml without embolization and 2800 ml after embolization with PVA particles. In our study, the average intraoperative blood loss ranged between 1550 ml in other tumors, 1775 ml in breast cancer metastases, 2500 ml in pulmonary tumor metastases and 3346 ml in renal patients who underwent a corpectomy or vertebrectomy. Nevertheless, it remains difficult to predict which spinal metastasis, apart from renal cell carcinoma, will be hypervascular. As shown in Fig. 2, spinal metastases of breast cancer may present a developed tumor vascularity. Imaging which enables to evidence the possible hypervascular character is therefore recommended in any type of tumor prior to major surgical interventions.

Prabhu et al. [8] report a positive predictive value of 77% of magnetic resonance imaging (MRI) in the determination of tumor vascularity. The criteria for hypervascularity include bright contrast enhancement, large signal voids representing blood vessels or the evidence of intratumoral hemorrhage, and arteriovenous shunts. However, hypervascular tumors may not be detected by standard MRI sequences. Spinal angiography allows determining the tumor vascularity as well as a possible relationship with the Adamkiewicz artery and radiculo-medullary arteries, which supply the anterior spinal artery [20]. Furthermore, angiography allows performing an embolization through the same procedure. Thus, angiography represents an appropriate procedure in any tumor type prior to complex surgeries such as corpectomy or vertebrectomy.

Conclusion

Preoperative embolization represents a valuable method which allows decreasing the risk of intraoperative hemorrhage in hypervascular spinal metastases such as renal cell carcinoma. A benefit of embolization could not be lined out for metastases of breast cancer and pulmonary tumors. The group of other metastases, especially thyroid carcinoma, needs to be further analyzed on a greater cohort. The extent of surgery remains an important risk factor for intraoperative bleeding. A preoperative angiogram should

be carried out in all types of metastases prior to a thoracolumbar corpectomy or vertebrectomy in order to perform an embolization if the tumor is hypervascular.

Disclosure of interest
The authors declare that they have no conflicts of interest concerning this article.

References
