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Neurosurg Clin N Am 15 (2004) 391–399

NEUROSURGERY
CLINICS
OF NORTH AMERICA

Embolization of metastatic spinal tumors

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There is potential for significant blood loss with resection of vascular metastatic spinal tumors, which may influence the surgeon's ability to have an adequate view of the surgical field, and thus to achieve a complete resection. Significant operative blood loss may be associated with increased requirements for transfusions, life-threatening hemorrhage at the time of surgery, longer operative times, intraoperative complications, postoperative intraspinal hematomas, and wound breakdown. Fortunately, preoperative embolization facilitates resection by decreasing intraoperative blood loss, improving visualization of the tumor during surgery, and decreasing the tumor size. Bhojraj et al [1] noted that the "bloodless field" with the use of preoperative embolization helps in an "unhurried decompression and satisfactory stable internal fixation."

Embolization is also effective as a primary treatment in symptomatic spinal metastatic lesions or in cases that are refractory to other treatment modalities, including surgery, irradiation, hormonal therapy, or chemotherapy. It is used as a palliative treatment in patients who are poor operative candidates or have recurrent, multiple, or unresectable tumors [2–9]. Embolization is used for the treatment of painful metastatic spinal disease [2–6,9,10] or for patients with neurologic compromise from metastatic lesions by reducing the tumor size, tumor growth, and spinal canal compromise [2,7–9].

Most series have focused on the embolization techniques for metastatic renal cell carcinoma, because approximately 70% of renal cell carcinomas are hypervascular [3,8,11–16]. It is important to note that there are many other vascular metastatic spinal tumors that have benefited from embolization procedures, including thyroid carcinoma, angiosarcoma, leiomyosarcoma, hepatocellular carcinoma, and neuroendocrine tumors (eg, pheochromocytoma, paraganglioma) [1,4–7,10,14,15,17–25]. Therefore, it is important to evaluate spinal metastatic lesions for potential benefits from primary or adjunctive embolization as part of a multimodality treatment approach.

This study reviews the larger series and important case reports regarding the indications, techniques, and outcomes for embolization of spinal metastatic lesions.

Technical considerations

There are many examples of patients undergoing surgery for metastatic spine lesions and requiring additional surgery because of excessive blood loss that could have been avoided by preoperative angiography and embolization [5,7,11,13,16,19,22,23]. If a vascular metastatic spinal lesion is suspected based on presentation, imaging, or a known history of primary malignant disease, preoperative angiography should be performed to demonstrate the hypervascularity of the lesion, to identify the main arterial feeders, and, ultimately, to determine whether the lesion would benefit from embolization [26]. Although most of the larger studies emphasize the embolization of

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1042-3680/04/$ - see front matter
doi:10.1016/j.nec.2004.04.003

renal cell carcinoma as described previously, many highly vascular spinal metastatic lesions may benefit from embolization techniques. Spinal angiography can determine a metastatic spinal tumor's potential benefit from an embolization procedure. Prabhu et al [24] reported that magnetic resonance imaging (MRI) is not always accurate in detecting the extent or lack of tumor vascularity (21% negative predictive value and 77% positive predictive value in determining vascularity), and thus is not a substitute for angiography. Overall, the indications for diagnostic spinal angiography and possible embolization are tumors of known vascularity or unknown primary origin regardless of MRI findings or MRI with signs of hypervascularity such as large flow voids, bright contrast enhancement, or evidence of hemorrhage [24].

A typical angiographic protocol is listed in Table 1 [5,23,27]. The intercostals or lumbar arteries are evaluated bilaterally at the affected vertebra (for thoracolumbar lesions), and, if possible, the vessels one or two levels superior and inferior are evaluated [5,8,14,21,23]. Angiography of a spinal renal cell or other hypervascular metastatic lesion typically demonstrates a hyperdynamic pathologic circulation within the vertebral tumor, enlarged feeding intercostal or lumbar arteries, angiographic blush caused by venous congestion within the tumor nidus (Fig. 1A), and, possibly, a rapid arteriovenous transit with early filling of draining venous channels [8,9,21,27,28]. The enlarged venous pools may contribute to a tumor's mass effect; therefore, embolization may decrease spinal cord compression [8]. Before embolization procedures, it is important to identify the segmental vessels that supply the spinal cord and the radiculomedullary branch of the anterior spinal artery and to determine whether an anterior spinal artery shares the same pedicle as the feeding artery of the tumor [5,11,21].

Table 1
Angiographic protocol for evaluation of metastatic spine lesions

Location	Evaluated arteries
Cervical	Vertebral, thyrocervical trunk, costocervical trunk, ascending pharyngeal, occipital
Upper thoracic	Supreme intercostal, thyrocervical trunk, costocervical trunk
Thoracic/upper lumbar	Intercostal or lumbar two levels above and below the lesion
Lower lumbar	Lower lumbar, medial and lateral sacral, iliolumbar

Embolization procedures are avoided if a lesion is hypovascular, which is confirmed by the absence of tumor stain on spinal angiography [4]. Additionally, embolization is difficult if there is atherosclerotic disease of the feeding vessels; if the feeding vessels are tortuous or hypoplastic; or if the tumor blood supply is in proximity to the anterior spinal artery, artery of Adamkiewicz, or other major feeding vessels to the spinal cord [4,19,20]. The presence of an anterior spinal artery at the same pedicle as the feeding artery of the tumor may be a contraindication for embolization [5,18,23]. There are reports of avoiding embolization in cases in which patients have a worsening neurologic examination and require immediate surgery, but Sundaresan et al [13] had complications relating to excessive blood loss in 7 of 13 patients (54%) who were rushed for emergency surgery for renal cell metastatic lesions without using preoperative embolization. In these cases, some authors advocate for delaying surgery for a few hours to perform preoperative embolization [13,14].

The choice of embolic material is based on the territory embolized, the vascular anatomy of the tumor, and the ability of selective delivery of an embolic agent via a catheter. Typically, polyvinyl alcohol (PVA) particles, Gelfoam (Pfizer, New York, NY), and coils are used, but other agents include tissue adhesive, ethanol, and microfibrillar collagen. Additionally, Courtheoux et al [2] treated patients with mitomycin C, a chemotherapeutic embolization material. The use of liquid agents intra-arterially, including ethanol, facilitates tumor necrosis but also has a higher risk of necrosis of normal tissue, including the spinal cord [28]. In a review of the literature, PVA was the most common material used as a single agent or in combination with other materials [4,5,7,8,12,15,16,18,21,23,24]. Generally, embolization is believed to be safe regardless of the agent used, but it is thought that embolization is ineffective if proximal occlusion of large vessels is performed without penetrating the distal tumor architecture [18,21].

PVA particles are commonly used for distal embolization to occlude vessels within the tumor [24,29]. These particles are inert, water insoluble, and nonabsorbable and occlude tumor vessels proximal to or at the capillary bed [18,23,24]. They are suspended in nonionic contrast material, which

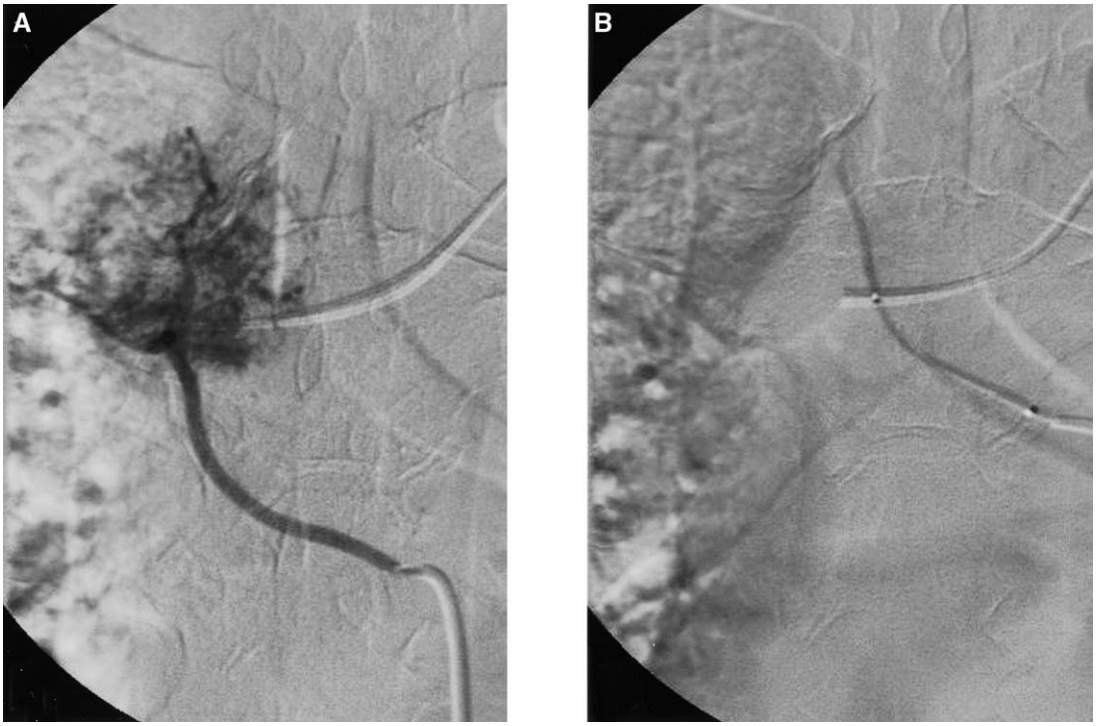

Fig. 1. (*A*) Spinal angiography of a T5 renal cell carcinoma metastasis demonstrating its tumor blush and feeding intercostal artery. (*B*) After embolization with polyvinyl alcohol particles, there is successful tumor devascularization with elimination of the tumor blush.

allows fluoroscopic visualization of their progress [24]. The particle size ranges from 45 to 500 μm [26]. Larger particles may be used when a shared blood supply is present to decrease the risk of spinal cord infarction or in patients who have undergone radiation therapy to reduce the chance of skin infarction [24]. Interestingly, Manke et al [15] showed that the size of the embolized PVA particle was not associated with a significant difference in intraoperative blood loss.

Gelfoam is a temporary occluding agent, it is degraded by enzymes, and recanalization typically occurs at 7 to 10 days [19,26,29]. Gelfoam is typically used as a temporary agent for protection of normal arterial branches during embolization of tumor feeders [18,23]. In the past, Gelfoam was used on its own for proximal occlusion of large vessels without penetration into the tumor, but this was ineffective because of early recanalization [18,23]. The use of Gelfoam particles for distal penetration is subject to rapid (within days) recanalization of the occluded vessel [4].

Coils are used for proximal occlusion and are effective because, unlike particles, they do not have the same potential for nontarget embolization; in addition, they are permanent [18,19,21]. Coils are also used to protect the origins of radicular vessels from embolization particles or to prevent segmental vessels from reflux of particles during embolization [3,15,24,29]. Coils are not always efficacious on their own, and most authors recommend using coils in conjunction with other embolic agents [21,24]. Of note, Berkefeld et al [21] found that there was not a statistically significant difference in blood loss in unembolized patients compared with patients who were embolized with coils alone. Significant differences in blood loss were found between the use of coils versus particles ($P = 0.025$) and coils versus particles plus coils ($P = 0.05$), however [21]. Interestingly, PVA particles compared with PVA particles plus coils had similar results in blood loss, and Berkefeld et al [21] hypothesized that after particle embolization, coils may offer no further benefit for reduction of blood loss.

Embolization procedures are usually performed under local anesthesia with intravenous sedation [5,15,19,23] or, in some cases, under

general anesthesia to limit patient movement or discomfort [11,24]. Most embolizations are performed in a single session and follow the diagnostic angiography [21,24], but there are reports of staged embolizations [18]. Some authors perform provocative testing or a "spinal Wada" test with lidocaine or sodium amobarbital to assess the risk of neurologic deterioration from embolization [5,9,18]. Others use neurophysiologic monitoring with somatosensory evoked potentials and motor testing [5,13]. It is important to realize that neurologic complications can occur in the absence of significant signal alterations when using neurophysiologic monitoring and that provocative testing may be limited by shunting of blood from the spinal cord circulation into the tumor bed and opening of collaterals during the embolization [21,24].

The goal of embolization is to occlude the blood supply to the tumor without compromising the blood supply to the spinal cord and normal tissue [28]. Selective vascular delivery of an embolic agent is desired to prevent constitution of collateral pathways and to minimize nontarget vessel occlusion and subsequent tissue infarction and necrosis. A coaxial catheter system is used to achieve a safe selective catheter position and to avoid embolization of the anterior and posterior spinal arteries [19,24,29]. The microcatheter tip is placed distal to the origin of a vascular branch supplying normal tissue so as to prevent nontarget embolization [28].

Superselective embolization may be difficult or impossible because of the numerous vascular channels or the size and course of the feeders. A potential solution is the use of blood flow–controlled techniques. These include preferential flow and flow reversal to ensure that the embolic agent flows toward tumor feeders, avoiding normal arteries. This technique avoids the opening of anastomotic channels that may be forced open when normal perfusion pressure is exceeded by pressure injection [21,23]. The flow-controlled technique can cause complications when the high-flow lesion is eliminated and embolic material flows to normal tissue through arteries that were previously not seen angiographically [28]. Frequent control angiography is performed during embolization to evaluate for opening of anastomotic pathways to the spinal cord and reflux of embolic material into normal arterial branches [14,23,28]. After the embolization is complete, the levels above and below the tumor are injected to evaluate for the reduction of tumor blush and presence of additional collaterals [21,28].

The number of vessels embolized depends on the arterial supply to the tumor and the safety of achieving complete embolization [24]. In the study of Prabhu et al [24], one (43%) or two (34%) segmental vessels were embolized in most cases, but there were cases of three (22%) or more vessels embolized. Others noted a mean embolization of 2 to 2.4 arteries [15,18].

The success of an embolization is judged by reduction in tumor vascularity and lack of tumor blush (see Fig. 1B) [1,17,23]. The percent reduction depends on the number of embolized arterial feeders to the tumor (failure to opacify on reinjection of contrast material) and the total number of feeders to the tumor [1,17]. Some groups reported angiographic success if there was greater than 75% obliteration of the tumor stain or if all pedicles were obliterated [4,15]. Complete embolization was achieved in 50% to 86% of studies [11,13,15,16,20,21,24], although there was variation in the definition of complete embolization between studies. Complete embolization typically could not be performed when the radiculomedullary artery shared the same vascular pedicle with the tumor [15,24]. Prabhu et al [24] approached this problem with superselective catheterization past the common pedicle, and they were able to perform 80% embolizations in 80% of patients.

The timing of surgery after preoperative embolization is an important technical consideration. Generally, it is recommended that embolization be performed as close as possible to the time of surgery. Typically, minimal blood loss occurs after embolization if surgery is performed within 24 to 48 hours after embolization [4,14,16,18–21,24,30]. Earlier surgery prevents the development of collateral circulation [19]. If surgery is delayed a week or more, some authors recommend repeat embolization [18].

Reduction of intraoperative blood loss

There are many reports of surgeries on metastatic renal cell carcinoma that were aborted because of "uncontrollable bleeding" or excessive blood loss in control groups that did not have preoperative embolization, whereas no cases were discontinued in patients who received complete preoperative embolization [5,7,11,12,15–17,19,22,23]. Many of these aborted cases were returned to

the operating room at a later date for successful surgery after undergoing preoperative embolization [5,11,13,16,17,22,23]. There are also reports of postoperative epidural hematomas [16,31], epidural hematomas causing paraplegia [14,19], and deaths caused by excessive blood loss [13,14,16] in patients who did not receive preoperative embolization.

Preoperative embolization of hypervascular metastatic lesions reduces intraoperative blood loss and improves the ability to resect the tumor, allowing more aggressive tumor resection. Sundaresan et al [12] noted that they were able to "perform gross total tumor resection without increased morbidity from excessive blood loss" with associated "improvement in survival and neurological palliation" in a series of patients with metastatic renal cell carcinoma to the spine treated with preoperative embolization. Preoperative embolization has been shown to reduce intraoperative blood loss for renal cell carcinoma; thyroid carcinoma; sarcoma, including angiosarcoma and leiomyosarcoma; neuroendocrine tumors, including paragangliomas and pheochromocytomas; and hepatocellular carcinoma [4–7,10–15,17–19,21–25]. These tumors are ideal candidates for embolization because of their large and accessible arterial feeders [24]. Other hypervascular metastatic tumors to the spine, such as multiple myeloma and melanoma, are not as amenable to embolization, because the main blood supply arises from a fine capillary network in the tumor and not from large segmental feeders [24]. Other common metastatic spinal tumors include breast, colon, and lung tumors, and they are relatively avascular [24].

Several authors have noted reduced intraoperative blood loss by one third to two thirds for metastatic spine lesions treated before surgery with embolization (Table 2). There are several other series with a low average blood loss of 870 to 1540 mL with embolization followed by surgery [1,17,23]. The blood loss that occurs after complete embolization is typically from large unembolized veins [21,24]. Hess et al [19] noted a significant difference between the amount of blood loss, intraoperative infusion volume requirement, and postoperative hemoglobin between embolized and nonembolized patients. Bhojraj et al [1] noted that the decreased blood loss associated with the use of preoperative embolization resulted in decreased time in surgery, averaging 3 hours for decompression and stabilization. Of note, two studies did not have significant differences in blood loss between the embolized and nonembolized groups [16,31]. Jackson et al [31] attributed their numbers to selection bias whereby the larger and more extensive tumors were referred for embolization, whereas the smaller and easier to resect tumors were not considered for embolization. In the study of King et al [16], 3 of 33 patients had significant intraoperative hemorrhages, and the authors noted that these complications could have been avoided with preoperative embolization.

Manke et al [15] found that even partially embolized renal cell metastatic lesions had significantly lower blood loss than nonembolized tumors ($P = 0.02$). Prabhu et al [24] and Manke et al [15] were not able to find a statistically significant difference between the extent of embolization and amount of intraoperative blood loss. In contrast, other authors have reported patients with excessive blood loss after partial or inadequate embolization, but factors other than the completeness of the embolization may have influenced these results [4,11,13]. Overall, it seems that it is best to attempt an embolization and even to obtain partial embolization of a hypervascular metastatic spinal lesion because of the low procedural complications, potential for significantly reduced blood loss, and increased ability to achieve total resection.

It is important to realize the limitations of using intraoperative blood loss as a parameter. Exact quantification of intraoperative blood loss is difficult, and estimates may vary between surgeons and anesthesiologists [18,21]. Also, the amount of intraoperative hemorrhage can vary on the basis of the relative vascularity of a tumor, the extent of operation, the tumor's location, the surgical approach, the fixation technique, and the surgeon's experience and speed. Significant blood loss may occur during the surgical approach or stabilization that preoperative embolization cannot prevent [21].

Palliation therapy

Embolization has also been used for symptomatic relief from metastatic disease as a primary treatment modality or in patients whose symptoms are refractory to other treatment options. Palliative measures are also ideal for patients who cannot tolerate a major surgical procedure because of multiple comorbidities or who have multiple metastatic lesions [9]. There is increasing literature

Table 2
Estimated blood loss after surgery in series reporting embolization and nonembolization numbers

Series	Number of cases		Embolization (mL)	No embolization (mL)	Significance
	Embolized	No embolization			
Roscoe et al, 1989	6	2[a]	3700	9000	NA
Gellad et al, 1990	14	10[a]	1850	>3500[a]	NA
Olerud et al, 1993	5	18	2200[b]	6400[b]	$P = 0.02$[b]
	6	NA	5100[c]	8200[c]	$P = 0.6$[c]
Hess et al, 1997	17	17	2088	3880	$P = 0.024$
Berkefeld et al, 1999	59	10	2195	5350	$P = 0.025$[d]
Manke et al, 2001	19	11	1500	5000	$P < 0.001$

Abbreviation: NA, not available.

[a] Includes patients with incomplete embolization and those in whom surgery was performed >3 days after embolization.

[b] Posterior surgery; number of cases.

[c] Anterior surgery; number of cases.

[d] Results were stratified: particles versus no embolization ($P = 0.025$) and particles plus coils versus no embolization ($P = 0.01$).

regarding the use of embolization for the treatment of pain [2–4,6–10] and for decreasing the symptoms from neurologic compromise [2,7–9]. Overall, with palliative therapy, surgical decompression may sometimes be delayed or postponed [4,5,7–9]. Although palliative embolizations may offer a patient relief of pain and neurologic symptoms, some patients eventually require surgery for spinal instability or continued tumor growth.

The mechanism of pain relief after embolization is not known. It is postulated that the pain relief occurs from the decrease in the size and growth of the tumor, which decreases the pressure of expansion or stretching of the periosteal nerve fibers responsible for pain [3]. Pain relief occurs at 12 hours to several days after embolization [3,6,7,9]. The temporary and palliative nature of the pain control may be related to the completeness of the occlusion and the availability of collateral circulation [3]. Two patients with metastatic renal cell carcinoma to the spine underwent embolization for pain control without further need for decompression therapy [4]. Breslau and Eskridge [5] had one patient who delayed surgery 1 month while her medical condition stabilized after embolization controlled her pain. Nagata et al [6] successfully treated patients with metastatic hepatocellular lesions, and all were free of pain by 1 week. There are also patients who do not get symptomatic pain relief after palliative embolization procedures [18].

Acute spinal cord compression from metastatic lesions is typically treated with radiation or surgical decompression, but there are examples of the use of embolization as an alternative or after the failure of radiation therapy. O'Reilly et al [8] treated three patients with embolization for solitary vertebral metastasis from renal cell carcinoma after radiation and steroids failed to improve the signs of acute spinal cord compression. All patients had neurologic improvement and pain reduction at 24 hours and progressive neurologic improvement that lasted longer than 3 to 9 months. All had significant improvement in strength and sensation, and two patients improved from paraparesis to ambulating with assistance. Kuether et al [9] treated a patient with acute spinal cord compression from metastatic renal cell carcinoma to the thoracic spine exclusively with embolization. The patient had decreased pain, increased strength, improved sensation, and decreased spinal cord compression on MRI. After 5 months of follow-up, the patient's lesion was stable in size and the patient did not require spinal decompression. Other metastatic spinal lesions, including thyroid carcinoma, can respond to the treatment of spinal cord compression with embolization therapy with rapid improvement of neurologic symptoms that lasts months to years [7].

Overall, patients can undergo repeat sessions of palliative embolization procedures as long as there is not an indication for surgical intervention [7,8]. Also, patients with multiple metastatic lesions can undergo embolization of several spinal lesions in one embolization session [7]. In the study reported by O'Reilly et al [8], two patients underwent repeat embolization after recurrence of symptoms because of acute spinal cord compression and had neurologic improvement.

Smit et al [7] described four patients who developed multiple metastatic follicular thyroid carcinoma lesions and underwent multiple embolization treatments.

Complications

Forty-three percent of patients experience a postembolization syndrome after any embolization procedure [32]. The syndrome includes malaise, nausea, emesis, low-grade fever, elevated white blood cell count, and local pain usually lasting 3 to 7 days [3,11,26,32,33]. Some patients experience transient (1–5 days) dorsal or lumbar pain that is thought to be secondary to tumor ischemia or necrosis [3,14,17,28].

Although most studies for embolization of spinal metastatic lesions did not have complications and the complication rate is low at 1% to 2% [3–5,7,11,14–17,19,20,23,24], several cases of neurologic compromise caused by tumor edema after embolization have resolved within hours to days or reversed after emergency decompression [9,11,13,18,21,31]. Many authors recommend periprocedural steroids to reduce edema [9,11,13,18]. Jackson et al [31] noted four serious complications in 47 patients treated with preoperative embolization (8.5%), with one case of permanent paraplegia, quadriparesis that partially improved in 2 patients, and aortic dissection that was successfully managed medically. It is important to recognize the potential for nontarget embolization and tissue ischemia; despite the low number of serious complications, embolizations of spinal metastases are technically demanding and necessitate the availability of an experienced interventionalist [11,19].

Other devascularization procedures

If a selective vascular embolization is not possible, direct percutaneous puncture techniques may be necessary [30,34,35]. Percutaneous intralesional injections of alcohol embolizing emulsions or N-butyl cyanoacrylate can be used when embolization is too risky because of proximity between the tumor's blood supply and the vasculature supplying neural tissue [30,34,35]. Tumor devascularization occurs by filling of the intratumoral vessels rather than by occlusion of the supplying pedicle, and it allows a complete filling of the vascular bed of the tumor. The procedure is performed with computed tomography or fluoroscopic guidance and contrast medium. The procedure is stopped after the embolic agent starts to inject the draining vein [35].

It is also possible to perform an intraoperative direct injection of an embolic agent [35,36]. Intraoperative direct injection of ethanol facilitates visualization and resection of spinal metastatic tumors by means of rapid devascularization and reduction of blood loss in patients with incomplete preoperative embolization or those who are unable to undergo embolization [36]. Lonser and colleagues [36] successfully treated two patients with metastatic renal cell carcinoma of the spine by slow incremental injections of small amounts of ethanol (0.1–0.2 mL) into the tumor. The end point for injection at a specific site was arrest of active hemorrhage with visible tumor blanching. The ethanol caused necrosis of the tumor, and the injected tissue instantly became soft and easy to resect.

Intraoperative cryosurgery is another method of devascularizing spinal metastases [37,38]. Freezing of the tumor causes immediate cessation of intratumoral blood flow and may allow better delineation of tumor planes [37]. Cryocoagulation is performed after adequate exposure of the tumor and separation of the tumor from the spinal cord [38]. Liquid nitrogen is the circulating agent with which freezing is induced. A probe is placed into the tumor, and the extent of cryocoagulation is controlled by intraoperative real-time ultrasonic imaging or by physical separation of the tumor from the spinal cord [37,38]. Nader and colleagues [38] used cryocoagulation to treat two metastatic renal cell carcinoma lesions to the thoracic spine and had blood loss of less than 500 mL in each case. They did not have complications attributable to the use of cryocoagulation, but freezing-related injury to the spinal cord is a risk.

Summary

Embolization is a safe and valuable primary and adjunctive treatment option for metastatic spinal tumors. Close consultation between the neurosurgeon, the oncologist, the radiation oncologist, and the interventionalist should lead to more applications of embolization techniques, thereby enhancing the treatment of metastatic spinal lesions. The development of newer embolic agents with chemotherapeutic properties should add to the efficacy of embolization for metastatic spinal disease [2].

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