

ARTERIAL EMBOLOTHERAPY

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Arterial embolotherapy, or embolization, is the selective endovascular occlusion of an artery or arterial bed. Successful embolization requires a thorough knowledge of arterial anatomy, embolic agents and delivery systems, as well as practical experience with the use of different types of embolic materials and catheters. The embolic agent of choice depends on whether temporary or permanent occlusion is desired and whether proximal or distal occlusion is required (see table).

Material	Duration	Location
Gelfoam	Temporary	Proximal to mid
Avitene	Temporary	Distal
Ethibloc gel	Temporary	Proximal, mid or distal
Occlusion balloon	Temporary	Proximal
Particles (PVA, Ivalon)	Permanent	Mid to distal
Spherical embolics (Embospheres, Contour SE PVA, Bead Block)	Permanent	Mid to distal
Coils	Permanent	Proximal, mid or distal
Detachable balloon	Permanent	Proximal
Sclerosants (sodium tetradecyl sulfate, sodium morrhuate, alcohol)	Permanent	Proximal, mid or distal
Thrombin	Permanent	Proximal, mid or distal
Glue	Permanent	Proximal, mid or distal
Onyx	Permanent	Proximal, mid or distal
Amplatzer	Permanent	Proximal to mid

Temporary (Reabsorbable) Materials

Gelfoam (absorbable gelatin sponge)

Gelfoam is one of the most widely used embolic agents and was previously available in both powder and sheet forms. Gelfoam powder measures 40-60 microns in diameter and produces a very peripheral occlusion. Because of this very distal level of occlusion, ischemic complications or frank infraction may occur with gelfoam powder, especially when non target embolization of normal tissue occurs. As of this writing, powdered gelfoam is no longer available and we will concentrate on the available sheet form. The sheets can be divided into pledgets and strips of various sizes. Small pledgets measuring 1-2 mm are utilized frequently. The strips are often compressed into the form of a cigar or torpedo and loaded in the nozzle of a 1 cc syringe. The gelfoam is then injected through the catheter using the hydrostatic force generated from the small syringe. A gelfoam slurry can also be made by shaving small pieces of gelfoam off of the sheet and suspending them in a mixture of contrast and saline either in a bowl or through a three-way stop cock between two syringes. This material can then be injected through the catheter. Gelfoam provides a temporary occlusion lasting approximately 3-6 weeks. In addition to producing mechanical occlusion of the vessel, it acts as a matrix for further thrombus formation. Inflammation of the

vascular wall can also occur and contributes to the vessel occlusion. Gelfoam is a non-toxic agent and recanalization of the vessel typically occurs within 5-6 weeks. This is extremely advantageous in situations where temporary occlusions are desired such as with pelvic trauma, priapism, peripartum hemorrhage, or possibly GI bleeding, especially from an ulcer.

When utilizing gelfoam, consider starting with a slurry to get a relatively arteriolar level of occlusion followed by gelfoam pledgets for a more proximal occlusion. The use of graded embolization with gelfoam minimizes the possibility of recurrent bleeding from reconstitution via collaterals. As noted earlier, the gelfoam pieces are injected with a small 1 cc syringe. Be cautious with the terminal injections of gelfoam because the sudden release of pressure as the gelfoam exits the catheter can lead to a very forceful injection with reflux of gelfoam into the parent vessel. This can result in significant non-target embolization.

Avitene (Microfibrillar Collagen)

Avitene is derived from bovine hide and works by causing mechanical occlusion, thrombus formation and severe granulomatous arteriolitis. The granulomatous reaction subsides in 2-3 months, at which time vascular recanalization will occur. Recanalization of larger vessels may occur in much shorter period of time. Avitene comes in a dehydrated form and is reconstituted with water-soluble contrast to achieve a pasty suspension or slurry which can be readily injected through a microcatheter. Because of its relatively small size, 50 - 150 microns, and the intense granulomatous arteriolitis it creates, Avitene can result in ischemic complications with associated extensive tissue infarction. Avitene is not utilized extensively as a routine embolic agent, although it may be used as a synergistic agent with other embolics. It should never be utilized with GI embolization and should be avoided in pelvic embolizations because of possible unintentional occlusion of arterial supply to the sciatic nerve.

Ethibloc Gel

This agent has been utilized extensively in Europe. It consists of an opaque, extremely viscous emulsion which can be injected through the catheter. Upon contact with an ionic solution such as blood, the material precipitates resulting in formation of a semi-solid substance. It consists of a solution of 65% alcohol containing corn protein, sodium amidotriosate and papaveris oil with some propylene glycol. Once the material precipitates, it creates mechanical occlusion of the vessel by creating a cast of the vessel itself. Ethibloc gel has been used in Europe for renal artery embolization as well as pelvic embolization. Within 6 months, the material will be reabsorbed and the vessel will recanalize.

Occlusion Balloons

Occlusion balloon catheters can be used to provide temporary occlusion of blood flow to a vascular bed, e.g. occlusion balloons placed in the internal iliac arteries can be inflated during delivery in patients who are at high risk for post-partum hemorrhage, or they can be used to prevent reflux of an embolic agent injected through the catheter tip beyond the balloon, e.g. pre-operative alcohol ablation of a renal cell carcinoma. The balloon should be sized appropriately to the vessel to be occluded and care should be taken to avoid overinflation, which may result in vessel injury or rupture.

Permanent (Non-Reabsorbable) Agents

Polyvinyl alcohol (PVA, Ivalon)

Polyvinyl alcohol was first utilized in foam form in the early 1970's. Currently, the material is available as particles ranging in size from approximately 50 microns to 2,000 microns, so the level of embolization can be tailored to the clinical scenario at hand. As with other very small particulate agents, the smallest size of PVA may result in significant tissue ischemia and should be reserved mostly for tumor embolization. PVA is delivered through the catheter in suspension form. The particles are mixed in a combination of saline and contrast either in a bowl or in syringes with a three-way stop cock. PVA has a tendency to flocculate or settle out of solution. Immediately prior to injection, the material should be resuspended so that uniform

injection can be obtained. Non-uniform delivery of the material can result in occlusion of the delivery catheter. Aggregation of PVA may result in a more proximal occlusion than intended. PVA causes direct mechanical obstruction and induces a foreign body type reaction with permeation of the particles by granulation tissue. Over time this reaction subsides and months to years later, the vessel may recanalize. Although PVA is considered to be a permanent agent, it will recanalize over time. PVA is utilized predominantly for tumor embolization as well as pre-operative devascularization of other lesions.

MicroSpherical Embolics

The goal of developing spherical embolic material is that it would overcome the limitations of PVA in regards to clumping and aggregation. This theoretically results in easier injection through microcatheters, more uniform distribution in the target vessels, and a more distal level of embolization. Differences among the size, distribution, compressibility, and deliverability result in more or less effective embolization, and allows for the savvy interventionalist to tailor the embolization particle to the indication. There are three products currently commercially available in the USA. Another embolic class, absorbable spheres, is currently being used outside the USA, and will be discussed as well.

Tris-acryl Gelatin Microspheres (Embosphere™, Embosphere Gold™) Biosphere Medical, Inc., Rockland, MA, www.biospheremed.com

Embosphere particles from Biosphere Medical are hydrophilic, Tris-acryl gelatin spheres. Available sizes range from 150 to 1200 microns, and they come in sterile vials or syringes, which are easy to use. Advantages of these particles are their compressibility. Less catheter clogging leads to less catheter exchanges due to occlusion. Better penetration of particles into the vascular bed allows for a more uniform embolization. Embosphere Gold™ is the same particle treated with gold colloid to impart a purple color, aiding in the visualization of the particle. Analysis of the distribution after embolization revealed Currently Embospheres have an FDA indication for uterine artery embolization in the treatment of fibroid disease.

Spherical PVA (Contour™) Boston Scientific, Natlick, MA, www.bostonscientific.com

Contour is a spherical form of the original particulate embolic, polyvinyl alcohol (PVA). Whereas original PVA was simply shaved, irregular particles, Boston Scientific developed a method called Matched Density™ Suspension in response to newer spherical agents. They come in sizes ranging from 45µm - 1800µm and are suspended in saline and contrast.

Acrylamido Polyvinyl Alcohol (Bead Block™) Biocompatibles, Ltd., UK, Farham, Surrey, www.biocompatibles.com

Bead Block™ is a PVA based microsphere manufactured using *N*-fil Technology™, originally a contact lens material. They are tinted blue like Embosphere Gold™ to aid in visualization. They come in pre-filled syringes and are reconstituted using saline and contrast.

Sulphonate modified N-Fil Hydrogel (LC Bead™, DC Bead™) Biocompatibles, Ltd., UK, Farham, Surrey, www.biocompatibles.com

A very new microsphere from the same company that makes Bead Block™, this embolic is cleared by the FDA for the embolization of hypervascular tumors and arteriovenous malformations. It's sister product, DC Bead™, has a special property that allows it to absorb chemotherapeutic agents for chemoembolization or other situations. This may impact the future of chemoembolization and usher in an age of drug-eluting beads.

Sodium Acrylate/Vinyl Alcohol co-polymer (HepaSphere™, QuadraSphere™) Biosphere Medical, Inc., Rockland, MA, www.biospheremed.com

Developed in 1996 by Hori et al in Japan, this microsphere comes in three different sizes. When exposed to aqueous solution (contrast/saline), the spheres swell up to 4 times the original diameter. It is a negatively charged polymer capable of bonding with positively charged material such as chemotherapeutic drugs. The company claims that it will conform to the vessel wall and even lodge at bifurcation points, molding to the angle. This property seems to result in a more distal embolization.

Which Microsphere to use?

A recent paper from Spain compared the three major microspheres with HepaSpheres™. They did a morphologic and histologic analysis in an animal model. They identified four properties of each material for comparison: 1) Particle Size, 2) Deformation (compressibility), 3) Number of particles present in the occluded vessels (measure of aggregation) and 4) Degree of distal embolization (proximal to distal embolization). The results are summarized in the table below:

Material	Mean Size (μm)	Deformation* (%)	Singularity** (%)	Zone of Embolization***
Embosphere™ 100-300 μm	132.9	18.1	59.1	Proximal – Mid
Bead Block™ 150-350 μm	108.1	16.5	91.1	Mid
Contour™ 150-350 μm	240.8	55.5	94.5	Proximal – Mid
Hepasphere™ 50 μm dry	225.3	26	94	Mid - Distal

* 100 X (largest diameter-smallest diameter)

** Percentage of occluded vessels with one particle each.

*** Proximal, Middle, Distal

Adapted from Bilbao, J.I., et al, *Comparative Study of Four Different Spherical Embolic Particles in an Animal Model: A Morphologic and Histologic Evaluation*, JVIR, 2008, 19:1625-1638.

Given these results, Embosphere™ had a small mean particle size, medium compressibility, a high incidence of aggregation, and a relatively proximal embolization. It did, however result in a permanent embolization with no recanalization at 4 weeks. Bead Block™ displayed good results in singularity and zone of embolization. It was as compressible as Embosphere™ but the mean particle size was smaller than the product stated. Contour™ was a relatively large mean size with little aggregation. It was, however, the most deformable of the particles. Most concerning, however, was the fact that there was almost full recanalization of the vessel at 4 weeks, suggesting this may not be a permanent embolic. Finally, Hepasphere™ resulted in the most distal embolization, low aggregation and low deformation. The difficulty in determining the size (dry vs. wet) may hamper its adoption. It is, however a very promising particle for effective embolization.

Coils

Coils are perhaps the second most common embolic agent utilized for percutaneous embolotherapy. Also identified as Gianturco-Anderson-Wallace coils after their inventors, coils consist of pieces of a stainless steel guide wire to which wool fibers are attached. Coils were used initially in the early 1970's. Since that time, numerous modifications have been made so that coils are available in almost all sizes from approximately 2 - 30 mm in diameter and are constructed of both stainless steel and platinum. Instead of the original wool, Dacron fibers are now present and woven into the coil to increase the thrombogenicity of the coil. In addition to direct mechanical occlusion by the coil, the Dacron fibers act as a nidus for thrombus formation. Extensive inflammatory changes are induced in the occluded arteries as well as in

the periadventitial tissue. Similar histologic findings are produced with coils containing either wool, silk or Dacron.

Coils produce a permanent focal occlusion leaving the vessel distal to the coils patent. The use of coils is analogous to a focal surgical ligature of the vessel. The size of the desired coil should be matched to the size of the vessel. If the coil is smaller than the vessel, the coil may embolize too far distally or through an AV fistula. Alternatively, if the coil is oversized, the coil may cause recoil of the delivery catheter with subsequent reflux of the coil back into the parent vessel. Also, an oversized coil may not assume its normal configuration which decreases the effectiveness of thrombus formation. Coils are not as innately thrombogenic as other embolic agents, and ancillary maneuvers may be necessary to optimize occlusion. These include placing a large coil and introducing smaller coils in the interstices of the larger coil or placing a large spider and nesting multiple coils within the larger spider. Also, delivery of coils followed by gelfoam followed by more coils ("gelfoam sandwich") enhances the effectiveness of vascular occlusion. Installation of thrombin into the coil delivery sheath ("soaking the coil") prior to delivery also enhances coil thrombogenicity by more rapidly and aggressively promoting thrombus formation on and around the coil.

The coils are advanced out of their carrier sheath into the catheter with the back end of the guide wire. The long floppy end of the guide wire (or a coil pusher wire in a microcatheter system) is then used to push the coil through the catheter and deliver it into the vessel. Microcatheter coils can also be injected with saline using 1 - 3 cc syringes.

One of the disadvantages of the coils is that once they are extruded from the catheter, they cannot be retrieved. Recently, the use of electrically detached coils as well as coils that can be detached mechanically have surmounted this problem. With retrievable coils, the coil can be delivered to its desired location to insure that it conforms appropriately to the vessel. If there is any reflux, recoil or malposition, the coil can be withdrawn back into the catheter and removed from the body.

Coils are utilized in almost any location where precise delivery of the embolic agent is necessary. Coil embolization has been described in almost every location and system within the body and in almost any clinical situation. Several caveats are important to keep in mind. In the setting of pelvic trauma, a temporary agent should be utilized as the initial agent and coils reserved for failure of the temporary agent. In the setting of AV fistulas, coils are superior to other particulate agents. With the reintroduction of detachable balloons, balloons may be more efficacious for AV fistulas.

Miscellaneous Permanent Agents

Numerous other particulate permanent agents have been described. These include silicon spheres, plastic or metallic pellets and spheres, nylon brushes, ferro magnetic particles, coated silk threads, and guide wire fragments. Due to problems with delivery or biocompatibility, many of these agents have not been widely utilized. Also many of these agents do not have significant advantages over pre-existing embolic agents and are mentioned only to give a sense of agents that have been tried in the past.

Balloons

Detachable balloons have recently been reapproved for vascular use and are extremely efficacious for high flow arterial venous fistulas. Balloons cause mechanical occlusion of the vessel with formation of thrombus proximal and distal to the balloon. Advantages include precise deployment and retrievability. Although the current balloons are made of silicon and may deflate over time, it is assumed that the vessel will remain permanently occluded because of the associated thrombus formation. Balloons are suitable for treating high flow pulmonary AVM's as well as a large vessel AVF's.

Sclerosant Agents

A wide variety of sclerosant agents are available and have been utilized in various clinical settings. Sclerosant agents include absolute alcohol; sodium tetradecyl sulfate (Sotradecol), which is an ionic detergent available in 1% or 3% solutions; and sodium morrhuate, which is utilized predominantly for

sclerosis of varicose veins and is a sodium salt of the fatty acids of cod liver oil. Other sclerosant agents that have been described include hot contrast medium which works but is extremely painful, hypertonic glucose solution and ethanolanime oleate. All sclerosant agents cause vascular occlusion from the level of obstruction to the capillary level and as such are extremely toxic and should be utilized carefully. They act by causing protein precipitation and destruction of the vascular endothelium. Most of these agents are utilized on the venous side.

Alcohol is utilized on the arterial side and should be used with extreme caution and probably only with occlusion balloons to prevent reflux of alcohol into the parent vessel. Because alcohol reaches the capillary level, it is an excellent agent for organ ablation or organ infarction. The corollary is that it also reaches the capillary level when a non-target embolization occurs and can cause extensive tissue infarction. The main use is for ablation of the kidney either pre-operatively or for functional ablation. When alcohol is injected into the main renal artery, it should be done with an occlusion balloon to prevent reflux into the aorta. As alcohol is less dense than blood, it will flow anteriorly and enter the first anterior vessel which usually is the inferior mesenteric artery. Reports of colonic infarction secondary to renal artery embolization with alcohol have been described. More and more data is accumulating that alcohol may be quite effective in treating arteriovenous malformations. Alcohol should be utilized in this setting only with significant experience.

Thrombin

Thrombin is a coagulation protein that converts soluble fibrinogen to insoluble strands of fibrin, causing effective clot formation. It is also known as activated Factor II (IIa). Thrombin is packaged in sterile powder form and is reconstituted commonly in 5,000 or 10,000 unit strengths. As thrombin is a potent thrombogenic material, it is commonly redistributed into 1cc aliquots containing 100 u. For most pseudoaneurysm applications, an injection of 0.2-0.5 cc (20 to 50 u) is sufficient for hemostasis. Thrombin is preferable for iatrogenic pseudoaneurysms of the femoral artery and other vessels, plus any other pseudoaneurysm that can be reached either by catheter or by direct needle placement. It can also be used to create autologous clot by mixing fresh blood with thrombin and amicar (aminocaproic acid). This can be a potent thrombosis platform. Other uses for thrombin include mixing it with microfibrillar collagen to create a slurry for topical hemostasis after dialysis graft intervention, oozing venous access sites, or post femoral artery cannulation. A popular product is D-Stat® Flowable Hemostat, which combines a kit including 5,000 u of thrombin and a vial of collagen. This can be stored in the IR suite, providing a convenient source of thrombin without having to consult the pharmacy.

Newer/Investigational Agents

PVA/PVAC Casting Agent

A solution of polyvinyl alcohol and/or polyvinyl acetate (PVAC) in an alcohol base is being considered for use and has been described in the animal model. Once this material is injected into the bloodstream, the alcohol diffuses out of solution allowing the polymer to precipitate again creating mechanical occlusion of the vessel. In the experimental work with PVAC, it is recommended that an occlusion balloon be used because of the very slow polymerization time. Much of this work is still experimental.

Onyx

Onyx (ev3, Irvine California) is the most recently developed liquid embolic agent. It is currently approved only for presurgical embolization of brain AVM's. Any other use is considered off label in the U.S., though there is growing literature supporting non-neurologic use. The agent consists of an ethylene vinyl alcohol copolymer dissolved in dimethylsulfoxide (DMSO). Micronized tantalum powder is added for radiopacity. The polymerization time is quite a bit longer than "glue" agents, which theoretically allows for a more controlled release of the agent from the microcatheter. The concentration of the copolymer dissolved in DMSO determines the viscosity of the substance. The different concentrations available in the U.S. include Onyx 18 and 34, which come in ready-to-use vials. The lower the amount of copolymer the less

viscous the agent, and the more distal penetration can be achieved in lower flow lesions. Conversely, a higher concentration of copolymer is preferred for high-flow lesions to provide for greater control.

The advantages of Onyx are related to its biologic activity. Its more gradual polymerization allows the user to inject it slowly over several minutes into a vascular lesion in a controlled manner. It is a viscous liquid that conforms to the shape of the blood vessels allowing penetration of the nidus that is observed fluoroscopically during the injection. Also, Onyx is nonadhesive, so there is much less risk of catheter tip retention compared with glue. The microcatheter does not need to be quickly removed after injection.

There are a few basic points for transarterial use that are unique to this agent. The microcatheter must be DMSO compatible. Once desired catheter position is achieved, the microcatheter is flushed with saline and then the 'dead space' of the catheter is filled with DMSO. Onyx is aspirated into a 1-ml syringe and injected slowly over 1 minute to fill the microcatheter and replace the DMSO. Onyx is injected under fluoroscopic guidance at a rate slow enough to prevent reflux around the microcatheter. If reflux is seen, the injection can be paused to allow for a "vascular plug" of Onyx to be formed at the tip of the microcatheter. Then the injection is continued, repeating these steps as needed. The benefit of greater penetration is weighed against the risk of continued reflux around the microcatheter. When an endpoint has been reached, slow continual force is used to withdraw the microcatheter. This can take several minutes in some instances, but is necessary to avoid catheter breakage.

The main risks of Onyx are similar to any embolic agent and are related to nontarget embolization and vessel occlusion. A unique risk of this agent is related to the DMSO, which can cause severe vasospasm and arterial wall injury if injected too quickly. Patient discomfort during injection of Onyx is also worse than with glue, and thus higher levels of sedation may be required. Increased cost and relative paucity of long-term data are other disadvantages compared with other embolic agents.

Amplatzer

The Amplatzer® Vascular (AGA Medical Corporation, Plymouth, MN) plug is a self-expanding nitinol mesh occlusion device. There are first, second and third generation devices available (although the 3rd generation is available only in Europe). This unique device shares a common heritage with atrial septal occlusion devices and has the advantage of stability in high flow lesions such as AV fistulae or AVMs. The device is detachable so that it can be redeployed for better positioning if indicated. One disadvantage is the need for a fairly large (5-6 fr) delivery guide catheter or sheath, which hampers distal embolizations. Nevertheless, this plug fills a void when you need occlusion in a very high flow system. Once expanded, it takes several minutes for complete occlusion, and may require the addition of traditional coils. It has been described as fairly effective in pulmonary AVMs, which are typically high flow lesions.

Tips on Catheter Systems for Embolization

In addition to selecting an embolic agent, a compatible delivery system must also be chosen. For example, gelfoam and large size PVA will quickly occlude the small lumen of a microcatheter. Similarly, catheters with side holes should be avoided because coils may exit through the side hole rather than the end hole and become stuck. Polyurethane catheters are incompatible with coils because their coefficient of friction is extremely high and coils may become stuck in the lumen. Hydrophilic catheters and microcatheters should be flushed well after each use to minimize friction as much as possible. In addition, frequent flushing of the catheter will also prevent occlusion of the catheter by the embolic agent. If coils will be delivered, it is useful to advance the pusher wire through the catheter to make sure that the catheter configuration is stable and that delivery of the coil will not cause dislodgement or recoil of the catheter. If coil injection is to be performed with a small syringe, it is important that the catheter is in an extremely stable position as forcible injection may cause recoil of the catheter. Any time embolization is being considered or performed, a sheath should always be inserted at the groin which will not only facilitate catheter changes but will also prevent loss of vascular access if the catheter becomes occluded by the embolic material.

As noted earlier, many patients who are bleeding briskly may have transfusion induced coagulopathies. In coagulopathic patients, thrombin stabilized clot or thrombin around the coils may enhance the thrombogenicity of the embolic agents. Ideally, embolization should be performed before coagulopathy occurs. If not, FFP and platelets should be administered along with packed RBC's. Close coordination with the clinical staff is necessary to insure that embolotherapy is considered early rather than late in the patient's clinical course.

Many of the embolic agents require arterial flow to deliver the material to the site of embolization. With catheter and guide wire manipulation, significant vasospasm may occur. A vasodilator such as nitroglycerine should be used liberally during the procedure to prevent or treat vasospasm.

Complications

Post embolization syndrome comprises a constellation of symptoms including pain, fever, nausea, vomiting, and leukocytosis. These symptoms are due to ischemia and possible infarction of the embolized organ. It is much more common with a solid organ embolization than embolization in other sites and is most pronounced with renal ablative procedures using absolute alcohol as the sclerosant agent. It is also quite common after uterine artery embolization as well as splenic embolization. With large solid organ embolization and with hepatic chemoembolization, prophylactic antibiotics are used to eliminate supra infection of the ischemic tissue. In many cases, it may be difficult to distinguish infection from the post embolization syndrome. If there is any uncertainty, one should obtain blood cultures and consider the use of antibiotics until the patient's condition stabilizes. Gas can be seen in infarcting tissue and is not, by necessity, a sign of infection. This is most commonly observed in necrosing liver lesions after hepatic chemoembolizations. The degree of pain is closely correlated with the amount of normal tissue that is involved in the embolization procedure and every effort should be made to spare normal tissue. The amount of pain should be anticipated and appropriate peri- and post-procedural analgesia should be administered. If necessary, epidural analgesia or PCA pump and/or nerve blocks should be considered before the procedure if a significant amount of pain is anticipated.

As post embolization syndrome is a common sequela of embolization procedures, it should not be considered a complication and this should be explained to the patient as well the nursing and other ancillary staff caring for the patient.

The most significant untoward complication of embolization is non-target embolization with unintentional occlusion of other vessels. This may occur when the embolic material passes through the vessel, which may occur with an AV malformation or AV fistula, or if the embolic material refluxes out of the embolized vessel into the parent or other adjacent vessels. As will be discussed later, adhering to appropriate technique during the embolization can minimize non-target embolization.

Some post-embolization complications may be caused by incomplete or suboptimal diagnostic angiography or inadequate evaluation of the vascular supply and collaterals before embolization. High quality diagnostic angiography is imperative. Angiographic tools such as road mapping can facilitate catheterization of complex vasculature. Both the primary supply and all collaterals to a source should be noted. The catheter should be advanced distal to any non-target vessel. In general, sequential selective angiograms are obtained until the catheter is in the desired location. Prior to embolization, an immediate pre-embolization angiogram is obtained with the catheter in its final position to insure that the catheter is in the desired vessel. Embolization of the wrong vessel may result in significant morbidity, as well as failure of the procedure.

There are several mimickers of active contrast extravasation that should be kept in mind any time a study is being done for bleeding. These include the adrenal blush, uterine blush, cavernosal blush and contrast in the renal collecting system. All of these normal structures may mimic contrast extravasation and these possibilities should be excluded to avoid embolization of a vessel that does not need to be treated.

Another factor that results in significant complications is use of an inappropriate embolic agent. Liquid sclerosant agents and small particles such as very small PVA or gelfoam powder should be used very carefully as they can cause occlusion to the capillary level with significant tissue infarction. Proximal

embolization with placement of a coil in a feeding vessel should also be avoided. Collaterals will reconstitute distal flow and placement of the coil in the feeding vessel will significantly hamper efforts to embolize the bleeding site through collateral vessels.

Again, thorough evaluation of the diagnostic arteriogram is of paramount importance. The most common etiology of embolization related complications is reflux of embolic material with subsequent embolization of the parent vessel or adjacent vessels. This is caused by a combination of factors which include inadequate selective catheterization, unstable catheter position, persistent injection of embolic agent after stagnant blood flow is present or a very vigorous forceful injection of the embolic material. Prior to embolizing, make sure that the catheter is in a stable position. This can be done by advancing the pusher wire through the catheter to insure that it does not dislodge the catheter or by vigorously injecting saline through the catheter to make sure that the catheter does not dislodge readily. Selective catheterization allows a further margin of error if there is inadvertent reflux of embolic material. For example, reflux from a selective injection in the uterine artery to posterior division branches will have a much smaller impact than reflux from the proximal internal iliac artery into the external iliac. The embolic agent should be delivered in a slow, controlled fashion in order to prevent reflux. Once stagnant flow is obtained and there is no further forward flow, particulate material should not be injected. This is especially true when using gelfoam, PVA or chemoembolization mixtures. Similarly, one should be prepared to retrieve any coil that inadvertently embolizes into a non-desired location or remains incompletely deployed with a portion in the parent vessel.

Clinical Scenarios

Upper GI Bleeding

GI bleeding has historically been divided into upper GI bleeding, proximal to the ligament of Treitz, and lower GI bleeding, distal to the ligament of Treitz, because of different etiologic, prognostic, and therapeutic implications. The most common etiology of upper GI bleeding requiring angiographic intervention is from ulcers nonresponsive to endoscopic maneuvers. Oftentimes embolization of the left gastric or gastroduodenal artery is required. Gelfoam is the favored material in the setting of upper GI bleeding. If the bleeding source is identified, a combination of gelfoam slurry followed by larger pledgets and torpedoes would be the optimal embolization technique. If there is an associated pseudoaneurysm, embolization should be performed on both sides of the pseudoaneurysm with coils.

If the patient has a history of prior surgery involving the upper GI tract, potential collateral sources could have been ligated and full diagnostic angiography should be performed to evaluate collateral supply to the bleeding territory prior to embolization. If there is limited collateral supply, an extremely selective embolization should be performed if at all possible. Duodenal embolization is technically more challenging because of the dual blood supply to the duodenum from the gastroduodenal artery as well as the inferior pancreaticoduodenal arcade (IPDA). As there are significant sources of collateral flow, proximal and distal embolization should be performed in the GDA. With any GDA embolization, an SMA injection should be obtained to ensure there is no collateral reconstitution to the embolized site from the IPDA. Very proximal occlusion with either coils or large particles of gelfoam may allow reconstitution of the bleeding site via collaterals.

There are certain situations where empiric embolization of either the left gastric artery or the gastroduodenal artery may be indicated. For the left gastric artery, this includes patients with a Mallory-Weiss tear or distal esophageal or fundal bleed that is not demonstrated angiographically. Similarly, if there is a documented duodenal ulcer that is bleeding intermittently, empiric embolization of the GDA can be performed.

Lower GI bleeding

Hematochezia or melena without associated hematemesis suggests a lower GI bleeding source.

Historically, lower GI bleeds have been treated with vasopressin infusion; however, recent evidence indicates that the incidence of enteric ischemia or infarction after embolization is very low. Therefore, embolization has now become the preferred means of treating lower GI bleeding. A variety of agents including Ivalon, gelfoam and coils have all been described for embolization of lower GI bleeds. Proximal embolization must be avoided and selective microcatheter catheterization is essential. An attempt should be made to advance the catheter as distal as possible - ideally to the level of the arcade where coils are then deposited. Vasospasm may be significant and routine use of vasodilators is beneficial. Vasopressin infusion should not be performed after an embolization as there is a significant risk of intestinal infarction with this combination.

Pelvic Embolization

The type of embolic agent to be utilized in the pelvis depends on the etiology of the bleeding. With pelvic trauma, the goal is to temporarily reduce the pressure head with cessation of bleeding. Gelfoam is the preferred agent and should be utilized initially. Coils are reserved for recurrent bleeding or persistent hemorrhage not controlled by gelfoam. Similarly, postpartum pelvic hemorrhage is best treated with a temporary agent. In these settings, prolonged attempts at subselective catheterization of bleeding sites are counter productive. There should be no hesitation to embolize the entire internal iliac artery if necessary. This is especially true when there are multiple punctate bleeding sites from various branches of the internal iliac artery. The goal is to rapidly stabilize the patient before they become hypothermic and coagulopathic, and the embolization should be performed in an expeditious manner.

When performing uterine fibroid embolization, selective catheterization of the uterine arteries followed by embolization using a spherical agent is the preferred technique. In patients that are bleeding from pelvic malignancies such as cervical carcinoma, embolization of any vessels showing hypervascularity should be performed. Occasionally, prepartum intervention is required for those patients at significant bleeding risk after a delivery or OB intervention. These include patients with placenta precreta or accreta or in those patients with unusual forms of ectopic pregnancy where hysterectomy frequently has to be performed. In these settings, placement of occlusion balloon catheters into both internal iliac arteries prior to delivery allows proximal vascular control by eliminating blood flow in the internal iliac arteries.

Hemoptysis/Bronchial Artery Embolization

Patients with chronic inflammatory conditions of the lungs, including cystic fibrosis, tuberculosis, and bronchiectasis, may suffer from severe hemoptysis. Bronchial artery embolization is the therapeutic modality of choice. Historically, bronchoscopy has been indicated to localize the site of bleeding. Several studies have shown that if the patient, especially in the cystic fibrosis population, can localize bleeding to one side, unilateral embolization of the involved side based on clinical signs alone will control the hemoptysis. In addition, any prior imaging studies including chest x-rays or CT's should be reviewed prior to the embolization as they may delineate the bleeding side.

It is extremely rare to identify frank extravasation from the bronchial artery and I do not rely on the presence of active extravasation to determine the need for embolization. Hypervascularity or enlargement of the arteries is enough to proceed with embolization. Reverse curve catheters are extremely helpful for selective catheterization of the bronchial arteries, and the use of a microcatheter is strongly encouraged. If a stable catheter position can be achieved with the base catheter, subselective catheterization with a microcatheter does not necessarily have to be performed, although one must be aware of the possibilities of reflux or nontarget embolization.

Numerous embolic agents have been described for bronchial artery embolization. Currently, a spherical embolic or PVA is the agent of choice, although large series have been described with the use of gel foam. Coils should not be used in the bronchial arteries as it is anticipated that repeat embolization will be required in the future because of the ongoing inflammatory condition in the lung. Use of coils increases the technical difficulty of future bronchial embolizations.

The presence of a spinal artery arising from the bronchial artery must always be evaluated prior to embolization. The presence of a spinal artery is not a contraindication to embolization. If a spinal artery is present, a microcatheter can be advanced distal to the origin of the spinal artery and embolization performed with very close fluoroscopic monitoring. Embolization of enlarged bronchial arteries may be sufficient to control hemoptysis. If the patient has rapid recurrence of hemoptysis, other arterial sources, such as internal mammary, intercostal or lateral thoracic arteries, that may be contributing to the bleeding should be evaluated and embolized if they supply areas of hypervascularity within the lung.

Pseudoaneurysms/AV Fistulas

Pseudoaneurysms and AV fistulas can occur throughout the body and are usually secondary to trauma, iatrogenic injury, infection or pancreatitis. When a pseudoaneurysm or AV fistula is identified, the vessel on both sides of the lesion should be embolized to prevent significant reconstitution of flow via collaterals. Coils are the preferred agent and should be deposited on both sides of the pseudoaneurysm or AV fistula or across the origin of the injured vessel. If the catheter cannot be advanced distal to the site of injured vessel, PVA can be injected to occlude the distal vessels followed by proximal occlusion using a coil. This is especially helpful in the hepatic or renal territories. Occasionally, a pseudoaneurysm may not be accessible angiographically and direct puncture of the pseudoaneurysm with thrombin injection may allow pseudoaneurysm treatment. If the patient is being evaluated for significant bleeding after placement of biliary or nephrostomy tube, the angiogram may need to be obtained with the catheter pulled back over a wire so that the catheter does not tamponade and obscure the bleeding site.

Spleen

One of the more common indications for splenic embolization is immediate preoperative embolization. This can be performed with either gelfoam or PVA injection followed by coils in the splenic hilum. The coils should not extend all the way back to the proximal celiac axis so that a portion of the splenic artery will be free of coils for intra-operative clamping. If the splenic embolization is being performed for reasons other than immediate preoperative splenectomy, prophylactic intravenous antibiotics should always be administered. Graded embolization is performed with Ivalon or gelfoam for thrombocytopenia. Occasionally, the entire spleen is embolized with Ivalon and coils to treat gastric varices where other alternatives are not possible. With splenic artery aneurysms, embolization should be performed with coils placed on both sides of the aneurysm.

Kidney

As with the spleen, one of the most common indications is preoperative embolization of the renal artery for resection of large renal cell carcinomas, especially when the renal vein is involved. Historically, this has been performed with alcohol; however, similar results can be obtained with fewer complications using gelfoam or PVA followed by coils. The coils should be appropriately sized to the renal artery and should not be placed in the proximal renal artery so that a portion of the main renal artery will be free of coils for intra-operative clamping.

In patients who are having ablation of the kidney due to unresectable tumors with pain or hematuria or for an ongoing nephrotic syndrome, alcohol is the agent of choice. Any time alcohol is used, an occlusion balloon should be placed in the renal artery to prevent reflux into the aorta. The occlusion balloon should be distal to the origins of the adrenal and gonadal arteries. The intra-arterial administration of lidocaine immediately prior to installation of alcohol may decrease the amount of post-embolization pain. When organ ablation is being performed, prophylactic antibiotics should be administered.

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