Embolization of the Internal Iliac Artery with Glubran 2 Acrylic Glue: Initial Experience with an Adjunctive Outflow Occlusive Agent

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The authors describe their initial experience with the adjunctive use of Glubran 2, a cyanoacrylate glue, in the embolization of the internal iliac artery (IIA). Glubran 2 was used in five patients as an adjunct to traditional techniques in the repair of isolated IIA aneurysms and to prevent retrograde perfusion of the aneurysm sac in the endovascular repair of aortoiliac aneurysms.

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Abbreviations: CIA = common iliac artery, IIA = internal iliac artery

EMBOLIZATION of the internal iliac artery (IIA) is indicated in the endovascular repair of isolated IIA aneurysms and as an adjunctive procedure in the endovascular repair of aorto-iliac and common iliac artery (CIA) aneurysms.

Isolated IIA aneurysms are rare (0.4% of all intraabdominal aneurysms) but dangerous, with a high incidence of rupture in untreated patients (67%) (1,2). The mortality following rupture is high (90%), principally due to the elusive nature of the symptoms and consequent delay in diagnosis and treatment (2). IIA aneurysms that cause pressure effects, such as compression of pelvic nerves, veins, the genitourinary tract, and the gastrointestinal system should also be repaired. Surgical resection and reconstruction of the IIA is technically challenging and requires thorough operative planning to avoid complications such as hemorrhage from pelvic venous injury and pelvic ischemia as a result of inadequate contralateral collateral pelvic blood flow (3). More recently, a variety of endovascular techniques have been applied in which coil embolization and endoluminal stent placement (often in combination) are used to treat isolated IIA aneurysms—with promising results (4).

Before endovascular repair of aortoiliac aneurysms (20% of abdominal aortic aneurysms) it is necessary to embolize the IIA to prevent retrograde perfusion of the aneurysm sac, which would otherwise result in a type II endoleak (5). Currently, the most definitive and recommended strategy is coil embolization of the IIA, which has been shown to be a safe and reliable technique (6). However, our experience and that of other authors have found that this can be costly and time-consuming (7).

Glubran 2 (GEM, Viareggio, Italy) is an acrylic glue that is licensed in Europe for endovascular use; it is not yet currently approved in the United States. Glubran 2 may be useful as an adjunct embolic agent in cases where complete occlusion of the IIA is proving time-consuming with standard techniques. Herein, we describe our technique of using Glubran 2 as an adjunctive occlusive agent for the IIA and report the outcomes in these patients as assessed with routine follow-up computed tomography (CT) and clinical review.

MATERIALS AND METHODS

A retrospective review was undertaken of all cases of IIA embolization performed at our institution between July 2007 and March 2008 in which management involved the use of Glubran 2 acrylic glue. Institutional review board approval was not required for this retrospective case review. During this period, five patients (all men; mean age, 77 years; age range, 72–84 years) had unilateral IIAs treated with Glubran 2. No patient underwent bilateral IIA embolization. The **Table** summarizes the indication, approach, embolization technique, and outcome in these cases. Glubran 2 was used in all cases to reduce the procedure time and provide a more effective outflow occlusion.

Diagnostic Evaluation

CT angiography helped confirm the diagnosis in all patients. All cases were for the elective treatment of large asymptomatic aneurysms detected either incidentally at imaging or at monitoring in a surveillance program. Three

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Summary of Indications, Procedures, and Outcomes

Patient No./Age (y)	Indication	Procedure	Outcome
1/79	Isolated left 4.6-cm IIA aneurysm	Ipsilateral approach Outflow: Glubran 2 (total volume with iodized oil, 2 mL) and coils* Sac and origin: Thrombin and coils*	Successful occlusion of the sac at postprocedure CT angiography and at 3 mo
2/78	Isolated left 5.2-cm IIA aneurysm	Ipsilateral approach Outflow: Glubran 2 (total volume with iodized oil, 3 mL) and coils* Sac: Thrombin Origin: Amplatzer vascular plug, 14 mm†	Successful occlusion at postprocedure CT angiography at 1 mo
3/84	Left 6.7-cm IIA aneurysm (small left CIA aneurysm)	Ipsilateral approach Outflow: Glubran 2 (total volume with iodized oil, 3 mL) Sac: Thrombin Origin: Amplatzer vascular plug, 14 mm†	Successful occlusion of the sac at postprocedure CT angiography and at 5 and 12 mo
4/72	4.4-cm left CIA aneurysm involving the IIA	1. Left IIA aneurysm embolization: Contralateral approach Inflow, sac, and outflow: Glubran 2 (total volume with iodized oil, 5 mL) alone; no coils or Amplatzer vascular plug required 2. Endovascular stent placement in the distal aorta and left CIA aneurysm‡	Successful stent placement and occlusion of IIA at postprocedure CT angiography and at 6 and 12 mo with no endoleak
5/73	5.3-cm infrarenal abdominal aortic aneurysm and bilateral CIA aneurysms. Left IIA had a dissection; decision was made to embolize the left IIA and preserve the right IIA	1. Left IIA embolization: Contralateral approach Outflow: Glubran 2 (total volume with iodized oil, 3 mL) Origin: Amplatzer vascular plug, 16 mm† 2. Endovascular aortoiliac aneurysm stent placement with stenting of the right IIA§	Successful stent placement with occlusion of the left IIA and patency of the right IIA at postprocedure CT angiography Type 2 endoleak from patent inferior mesenteric and lumbar arteries Stable appearances of the endoleak and left IIA occlusion at CT angiography at 3, 6, and 12 mo

Note.—All patients were men.
* MReye embolization coils and Tornado embolization microcoils platinum (Cook, Bloomington, Indiana) were used.
† AGA Medical, Plymouth, Minnesota, manufactures the Amplatzer vascular plug.
‡ An 81 × 20-mm Aorfix endovascular stent-graft (Lombard Medical, Didcot, Oxfordshire, United Kingdom) was used.
§ The Zenith Flex abdominal aortic aneurysm endovascular graft (Cook), which has a bifurcated main body with iliac legs, was used. A 13.5 × 40-mm Fluency Plus stent-graft (Bard, Crawley, West Sussex, United Kingdom) was placed in the right IIA.

patients had an isolated IIA aneurysm, one patient had a CIA aneurysm involving the IIA, and one patient had an abdominal aortic aneurysm and bilateral CIA aneurysms.

Before performing endovascular therapy, we assessed the contralateral circulation with CT angiography for evidence of stenosis or occlusion to determine the risk of pelvic ischemia. The contralateral IIA was normal in all cases. Informed consent was obtained from all patients after we explained the rationale for treatment and how this outweighed the risk of complications, including the development of severe pelvic ischemia as a result of the procedure.

Access Technique

Ipsilateral or contralateral approaches were used depending on the operator-subjective assessment of the anatomy of the common iliac and internal iliac bifurcations. With use of a standard Seldinger technique, a 6- or 8-F sheath (Cordis, Johnson and Johnson, Miami, Florida) was placed into the femoral artery and the IIA selectively cannulated by using a 4-F Terumo cobra catheter and 0.35-inch curved Terumo guide wire (Terumo, Tokyo, Japan). This was exchanged over an Amplatz Superstiff wire (Boston Scientific, Natick, Massachusetts) with either a 6- or 8-F hockey stick guiding catheter (Cordis, Johnson and Johnson), which was then placed 2–3 cm into the IIA or IIA aneurysm. A Tuohy Bohrst adapter (Cook) was placed and the 4-F glide cobra catheter re-introduced over the wire. The Terumo cobra catheter was used for embolization in four patients and a Progreat microcatheter (Terumo) was used in one patient.

Glubran 2

Glubran 2 is different than other cyanoacrylate glues on the market (eg, Histoacryl; B. Braun, Melsungen AG, Germany) because its chemical compo-

sition consists of a co-monomer rather than a simple monomer of *n*-butyl cyanoacrylate. Glubran 2 consists of *n*-butyl cyanoacrylate modified by the addition of a proprietary monomer synthesized by the manufacturer. This allows Glubran 2 to polymerize with a smaller exothermic reaction (45°C) and bestows a substantial anti-inflammatory effect, which may help limit procedure-related endothelial cell damage (8). Glubran 2 also has a slightly longer polymerization time, which might allow easier application of the glue in the endovascular setting—where there remains concern about catheter fixation (8). The glue starts to set on contact (after 1–2 seconds) with ionic substances such as blood or saline, completing the setting reaction after 60–90 seconds. The exact polymerization time depends on the type of tissue with which the glue comes into contact and the concentration of the glue applied. To aid fluoroscopic visualization, the glue can be diluted with iodized oil (Lipiodol; Laboratoire Guerbet, Roissy-Charles-de-Gaulle Cedex, France) in various ratios such as 1:1, 1:2, and 1:3 on the basis of the morphologic features of the case and individual blood flow.

Embolization Technique

Before its use, each 1-mL vial of Glubran 2 was mixed with 2 mL of iodized oil to give a ratio of 1:2. Glubran 2 polymerizes rapidly once in contact with ionic substances such as blood or saline. The catheter used during the procedure was flushed with 5% dextrose solution before injection of Glubran 2 to remove all traces of blood and saline. A three-way tap was attached to the end of the catheter, with the direct-flow channel used for the injection of Glubran 2 and the side port available for flushing with 5% dextrose. In each case, one or two vials of the glue–iodized oil mixture was injected in a continuous column with the flow rate of glue monitored by means of continuous fluoroscopy. This provided visual feedback to manually alter the injection rate as required. Contrast medium was injected through the guiding catheter to evaluate success, with the endpoint of embolization determined as the absence of antegrade flow in the IIA outflow. To avoid retrograde spillage, the catheter was positioned well within the aneurysm sac. After satisfactory IIA outflow occlusion, approximately 1–2 mL of human thrombin (500 IU/mL Tisseel Lyo; Baxter, Vienna, Austria) was injected in the center of the aneurysm sac through either the microcatheter or the 4-F cobra catheter to ensure rapid sac thrombosis.

Patients 1 and 2: Isolated IIA Aneurysms

Initial embolization of the aneurysm outflow was performed with coils. The operator decided to use Glubran 2 as an adjunct to aid embolization of the outflow because of the lengthy procedure and poor initial results with coil embolization (see the **Table** for details of coils). With the catheter tip placed at the origin of the aneurysm outflow, Glubran 2 was injected by using a steady and slow technique, with continuous fluoroscopic screening to monitor the localization of the glue within the target vessel. In both cases, Glubran 2 was seen to remain within the aneurysm outflow and none was seen to penetrate into the more distal IIA branches as determined with fluoroscopy. For the aneurysm sac, we injected 1–2 mL of thrombin, which achieved rapid occlusion in both cases. For the origin of the IIA aneurysm guided by the morphology of the vessel, we deployed standard coils in patient 1 and the Amplatzer vascular plug in patient 2. Successful occlusion of the aneurysms was confirmed with angiography.

Patient 3: Isolated 6.7-cm IIA Aneurysm

With use of the technique described, one vial of Glubran 2 without any coils was used to successfully embolize the aneurysm outflow. Complete occlusion was achieved with 1 mL of thrombin injection in the sac and an Amplatzer vascular plug at the IIA origin (**Fig 1**).

Patient 4: Isolated 4.4-cm CIA Aneurysm Involving the IIA

The IIA aneurysm was embolized before placement of an aortoiliac stent-graft. With use of a careful technique, the IIA aneurysm outflow, sac, and inflow were successfully embolized with Glubran 2 alone, without the need for thrombin or adjunctive devices (**Fig 2**). During this procedure, technical success was achieved quickly with Glubran 2 alone and without any complications such as distal flow of glue at fluoroscopy. We waited 3 days before placing an endograft in the CIA aneurysm to ensure adequate occlusion of the IIA had occurred (**Table**; Aorfix) and to ensure there were no significant ischemic complications after the procedure.

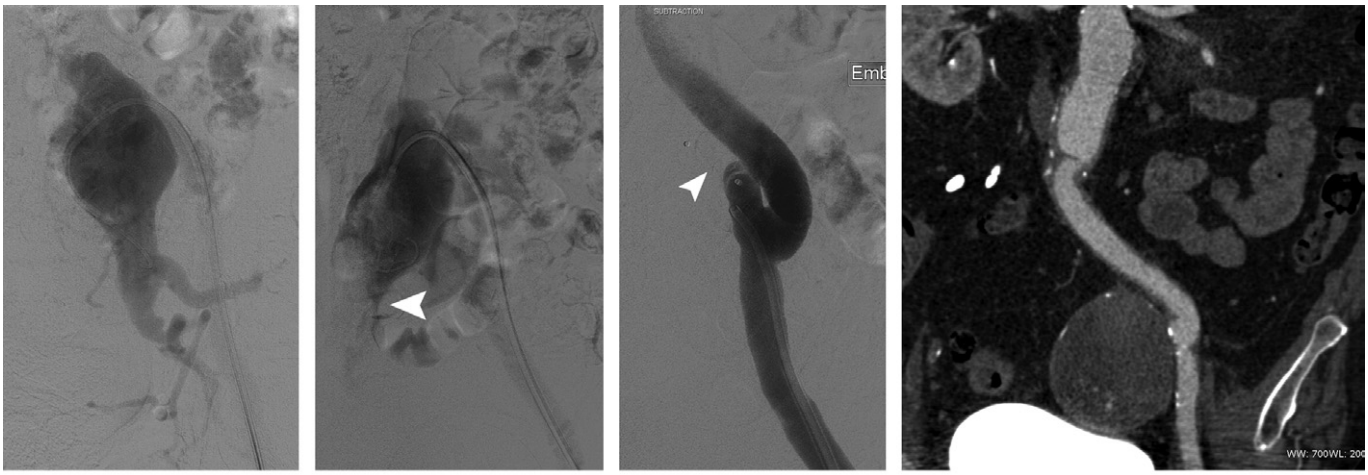
Patient 5: 5.3-cm Infrarenal Abdominal Aortic Aneurysm Extending to Bilateral 4-cm CIA Aneurysms

Preprocedure CT angiography depicted a chronic dissection within the left IIA, which was not aneurysmal, and a normal right IIA. We embolized the left IIA to prevent endoleak but preserved contralateral pelvic blood flow by placing a stent in the right IIA with use of a branched aorto-bi-iliac graft. Initial embolization of the left IIA was performed with Glubran 2 as previously described. Satisfactory occlusion of the IIA following deployment of an Amplatzer vascular plug at the IIA origin was confirmed with digital subtraction angiography. The patient proceeded to undergo placement of a stent-graft 3 days after IIA embolization (**Table**).

RESULTS

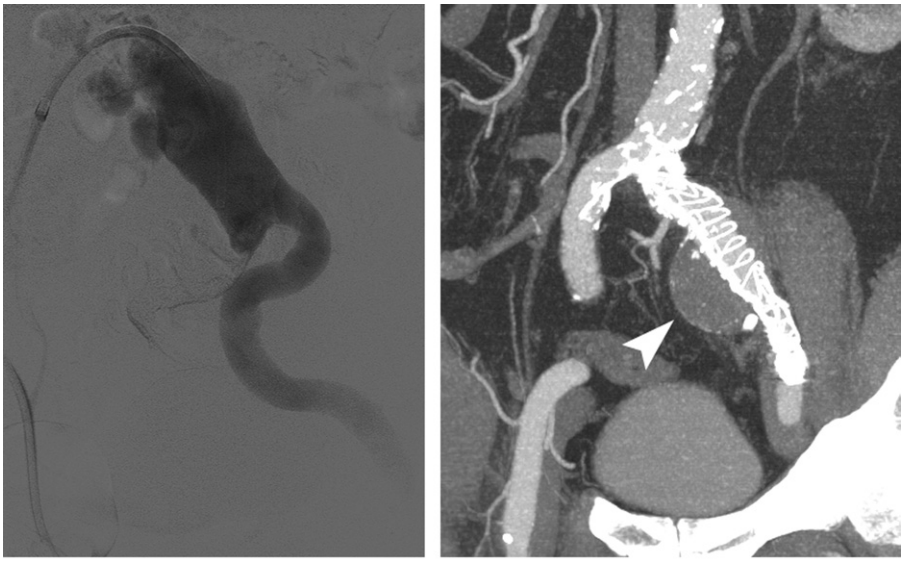
All three cases of isolated IIA aneurysms were successfully embolized, as determined with postprocedure CT angiography and CT angiography performed at short-term follow-up (range, 1–12 months; mean, 5.3 months). There were no immediate or delayed complications in these patients (**Table**). Clinical review was satisfactory in all patients, with no symptoms of pelvic ischemia reported.

Patients 4 and 5 both had successful embolization of a left IIA before aortoiliac stent placement and complete occlusion at immediate and 12-month follow-up CT angiography. In both cases, the patients reported mild claudication in the ipsilateral buttock and thigh immediately after the embolization of the IIA (patient 4 was symptomatic after walking 500 m and patient 5 was symptomatic after walking 250 m). Formal treadmill tests were not performed. There were no reported symptoms of neurologic or colonic ischemia or sexual dysfunction. These symptoms were attributed to a mild degree of pelvic ischemia and were managed conservatively. The claudication remained persistent at



a. b. c. d.

Figure 1. Patient 3. Images in an 84-year-old man with a small left CIA aneurysm extending to a 6.7-cm IIA aneurysm. This patient had previously undergone endovascular repair for a ruptured abdominal aortic aneurysm with a simple aortic tube graft due to difficulties at surgery. It was decided to carry out an endovascular repair of the left IIA aneurysm. **(a)** Digital subtraction angiogram of the left IIA aneurysm. **(b)** The Glubran 2 mixture was injected into the distal part of the aneurysm so that arterial flow could distribute it into the outflow vessels. Image from digital subtraction angiography shows complete occlusion of the outflow vessels of the left IIA (arrowhead). **(c)** After thrombin injection in the sac, an Amplatzer vascular plug device (14 × 10 mm) was deployed at the origin of the aneurysm, resulting in successful occlusion of the inflow (arrowhead). **(d)** Postprocedure CT angiogram helps confirm successful occlusion of the IIA aneurysm with no endoleak.



a. b.

Figure 2. Patient 4. Images in a 72-year-old man with a 4.4-cm isolated left CIA aneurysm extending to the IIA. Before stent placement in the CIA aneurysm, the IIA required embolization to prevent endoleak. **(a)** The IIA aneurysm and its outflow were selectively embolized with complete occlusion by using Glubran 2 alone. **(b)** Standard endovascular repair of the left CIA aneurysm with a stent-graft deployed across the distal aorta and left CIA was performed 3 days later. Maximum intensity projection image from postprocedure CT angiography helps confirm successful stent placement and occlusion of the IIA aneurysm (arrow).

short-term follow-up of 6 months. Contralateral IIA flow in these two patients was normal at CT angiography performed before and after the procedure (the contralateral IIA was stented and remained patent in patient 5). Patient 4 had narrowing in the distal part of the stent in the external iliac artery, but a good femoral pulse was palpable. This may have reduced collateral blood flow from external iliac artery branches and contributed to ischemia. Similarly, in patient 5 the infrarenal aorta and both CIAs were stented; therefore, collateral flow from lumbar branches might have been reduced. The inferior mesenteric artery was patent in this case, causing a type II endoleak.

DISCUSSION

Currently, cyanoacrylates are the most common adhesive used in endovascular procedures, being most widespread in neurointervention where they have been shown to be relatively safe and efficacious—particularly in the embolization of cerebral tumors and arteriovenous malformations (9). In recent years, their use in peripheral embolization has become more extensive, with a wide range of applications being developed—including the embolization of pelvic arteriovenous malformations and the treatment of posttraumatic priapism (10,11).

Current practice in the embolization of isolated IIA aneurysms and in the embolization of the IIA before placement of an aortoiliac stent-graft is to use multiple coils (6,12). However, for IIA aneurysms it is important to treat the

outflow to prevent retrograde filling of the sac. This requires selective coil embolization of multiple vessels, which can be time-consuming in some cases. In cases of IIA embolization before endovascular aneurysm repair, the aim is tight packing of the IIA with coils above its bifurcation to achieve a proximal embolization. The risk of pelvic ischemia is increased if coils are deployed at or distal to the bifurcation rather than in the proximal IIA (6). Inaccurate embolization of the IIA can be complicated by coil migration, which has been reported to occur in 20% of cases (7). Unintentional placement of coils in distal branches of the IIA can lead to compromise of the collateral pelvic circulation and cause pelvic ischemia (13). Other authors have favored balloon embolization or surgical approaches such as IIA ligation, with some advocating that IIA embolization is unnecessary if the IIA orifice is small (14–16). The recent development of the Amplatzer vascular plug has improved the ease and efficiency of IIA embolization, being particularly suited in our experience to occlusion of the origin of the IIA, and has been described successfully in IIA embolization (7,17). One of the drawbacks is that its cylindrical shape is more suited to a short portion of blood vessel with a constant diameter; a tapering vessel may be more amenable to traditional coil deployment (7).

We present a small retrospective case series of five cases where the acrylic glue, Glubran 2, was used successfully as an adjunct to the traditional embolic agents, coils, thrombin, and the Amplatzer vascular plug and in one case as the sole embolic agent in endovascular embolization of the IIA. Our initial experience has highlighted the advantages and disadvantages of this material. Technical success was achieved in all five patients who underwent IIA embolization with use of Glubran 2, with complete occlusion of the IIA at short-term follow-up CT angiography (range, 1–12 months; mean, 8 months). Although the patient who underwent endovascular aneurysm repair developed a type 2 endoleak, this did not originate from the successfully embolized IIA. Before the study period, our department did not have access to Glubran 2 and previously we had performed endovascular embolization of similar aneurysms with a combination of coils, the Amplatzer vascular plug, and thrombin.

Glubran 2 was primarily used as an adjunct to coils to occlude the IIA outflow and not the aneurysm sac. We decided to use thrombin in the sac because it is an extremely potent enzymatic agent, and in our experience only a very small volume (1–2 mL) is sufficient to achieve rapid occlusion, rather than the much larger volume of Glubran 2 that would be required to fill the whole sac. Although thrombin has risks of anaphylaxis, this is reduced if using human thrombin as used in our institution rather than bovine thrombin. Thrombin has a small but serious risk of vessel thrombosis outside the target vessel.

The major concern with any liquid glue is the risk of propagation of glue more distal than the intended target; for example, it might migrate more distally within the IIA than anticipated, occluding the vascular bed and causing ischemia. There is also the risk of uncontrolled migration into nearby vessels. This feature makes it more challenging in less-expert hands. Despite a careful embolization technique with Glubran 2, both of our patients who underwent treatment before placement of an endovascular stent-graft developed new-onset mild buttock claudication ipsilateral to the side of the IIA embolization (both were symptomatic after walking distances of more than 250 m). In both cases, Glubran 2 was used to occlude the IIA without any coils, although an Amplatzer vascular plug was used at the origin in the patient treated before endovascular aneurysm repair. However, this is a common complication after unilateral IIA coil embolization, with a reported incidence of around 35% of moderate to severe claudication (symptoms on walking less than 250 m on level ground) in a series of 46 patients (6). Another study reported symptoms of buttock claudication in 30% of patients undergoing coil embolization of the IIA and in 40% ($n = 5$) undergoing embolization solely with the Amplatzer vascular plug (7). In our report, 40% of patients had mild claudication after the procedure, which is comparable. The small numbers in our study make it difficult to draw significant conclusions as to whether patients treated with Glubran 2 have a similar or higher risk of developing pelvic ischemia, and larger prospective studies are required. Although we did not see distal propagation of Glubran 2 it is possible that embolization occurred more distally than was appreciated at angiography. Both our cases have only had a 6-month follow-up. Many patients' symptoms resolve at long-term follow-up due to the development of collateral pathways (18).

Unlike coils, embolic glues do not require an adequate level of patient clotting factors to cause embolization. Another advantage of Glubran 2 is its low cost. In this small retrospective series, we did not do a full cost analysis. A single 1-mL vial of Glubran 2 costs our department $160 and was sufficient for one case. In their study examining IIA embolization before aortoiliac repair, Ha and Calcagno (7) calculated the cost of coil embolization in 10 consecutive patients followed by the Amplatzer vascular plug alone in five consecutive patients. With use of either Tornado or Nestor embolization coils (Cook) at an average cost of $400–$600 each, they estimated that the average total cost of coils per IIA was $3,500, with an Amplatzer vascular plug costing only $375. From our limited experience with Glubran 2, we were able to use fewer coils than we would have used previously.

An alternative liquid embolization agent is Onyx (ev3, Plymouth, Minnesota), which has been reported in the treatment of an IIA aneurysm (19). It is non-adhesive, with the advantage of a reduced risk of catheter fixation. However, there remains limited experience with its use in peripheral embolization and it is expensive, costing our institution $760 for one vial.

In conclusion, we present a small, retrospective report of our initial experience with Glubran 2 as an adjunct embolic agent in the embolization of the IIA. In our experience, the technical procedure is relatively straightforward. However, Glubran 2 should be used with caution until larger prospective studies have evaluated its safety with respect to the risks of pelvic ischemia. Although we only have results from short-term follow-up, IIA embolization was successful in all cases and there were no serious complications. Further studies should evaluate the future role of Glubran 2 in the treatment of IIA embolization.

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