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Angiología

Revisión

Effectiveness of the Amplatzer™ vascular plug versus gelatin sponge particle instrument on transarterial embolization of renal tumors to improval surgical outcomes: literature review

Efectividad del tapón vascular Amplatzer™ frente al instrumento de partículas de esponja de gelatina en la embolización transarterial de tumores renales para mejorar los resultados quirúrgicos: revisión de la literatura

Lalu Muhammad Sabar Setiawan, Yan Efrata Sembiring

Departement of Thoracic, Cardiac and Vascular Surgery. Faculty of Medicine Dr. Soetomo. General Hospital. Universitas Airlangga. Surabaya, Indonesia

Abstract

The recommended first-line therapy to replace open surgery of renal tumors is endovascular management through percutaneous transcatheter embolization. The use of Amplatzer™ Vascular Plug (AVP) and Gelatin Sponge Particles (GSP) for endovascular procedures has been widely reported and many have reported successful.

A literature search was conducted using the PubMed, Embase, and Science Direct databases published between 2014-2021. Keywords used for searches included renal cancer, transarterial embolization, Amplatzer Vascular Plug and Gelatin Sponge Particles.

Several studies reported that AVP is more effective than GSP. AVP causes total occlusion compared to GSP, resulting in long-term incomplete recanalization. The clinical symptoms after using AVP agents are minimal compared to GSP. AVP has the ability to place agents in places of tortuous and difficult blood vessels while GSP is still difficult in this regard. The complications after using AVP are minimal compared to GSP which has high complications.

In several case reports, the use of AVP is effective and safe on transarterial embolization procedure for renal tumors. AVP is very effective in use, especially in cases associated with peripheral renal artery structures. Using GSP requires a long time and also requires recanalization. To achieve partial recanalization and complete thrombus, 4 weeks post-embolization with GSP is required.

Keywords: Renal cancer. Embolization. Amplatzer™ vascular plug. Gelatin sponge.

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Correspondence:

Yan Efrata Sembiring. Departement of Thoracic, Cardiac and Vascular Surgery. Faculty of Medicine Dr. Soetomo. General Hospital. Universitas Airlangga. Surabaya, Indonesia
e-mail: yan-e-s@fk.unair.ac.id

Abstract

La terapia de primera línea recomendada para reemplazar la cirugía abierta de tumores renales es el manejo endovascular mediante embolización percutánea transcatéter. El uso de Amplatzer™ Vascular Plug (AVP) y partículas de esponja de gelatina (GSP) para procedimientos endovasculares se ha estudiado ampliamente y muchos autores han comunicado resultados exitosos.

Se realizó una búsqueda bibliográfica utilizando las bases de datos PubMed, Embase y Science Direct publicadas entre 2014-2021. Las palabras clave utilizadas para las búsquedas incluyeron cáncer renal, embolización transarterial, tapón vascular Amplatzer™ y partículas de esponja de gelatina.

Varios estudios ha informado de que AVP es más eficaz que GSP. La AVP causa una oclusión total en comparación con la GSP, lo que resulta en una recanalización incompleta a largo plazo. Los síntomas clínicos después de usar agentes AVP son mínimos en comparación con GSP. AVP tiene la capacidad de colocar agentes en zonas de vasos sanguíneos tortuosos y difíciles, mientras que GSP sigue mostrando más dificultades en este sentido. Las complicaciones después de usar AVP son mínimas en comparación con GSP, que tiene muchas complicaciones.

En varios estudios de casos, el uso de AVP es eficaz y seguro en el procedimiento de embolización transarterial para tumores renales. La AVP es muy eficaz en su uso, especialmente en casos asociados con estructuras de la arteria renal periférica. El uso de GSP requiere mucho tiempo y también requiere recanalización. Para lograr una recanalización parcial y un trombo completo se requieren 4 semanas posembolización con GSP.

Palabras clave:
Cáncer renal. Embolización. Tapón vascular Amplatzer™. Esponja de gelatina.

INTRODUCTION

One of the most prevalent tumors, renal cancer, also known as Renal Cell Carcinoma (RCC), mostly affects people over the age of 50 (1). On a global level, the frequency of this has increased. According to GLOBOCAN, renal cancer cases were 431,288 in 2020 or 2.2 %, and RCC fatalities were 179,368 in total or 1.8 % (2). In the United States, the tenth-largest cause of cancer death in adult men is RCC. Based on GLOBOCAN data from 2012, the death rate for men with renal cancer in Indonesia was 1.6 per 100,000 and 0.8 per 100,000 for women (3). While the rate of RCC increased, there was also a 20-30 % increase in metastases. The use of computed tomography imaging for other illnesses, which improves the detection of renal tumors detected by accident, is to blame for the rise in RCC instances.

Initially used to treat untreatable renal cancer that was accompanied by symptoms, renal artery embolization is now more frequently utilized to support surgical resection in patients with renal tumors. Since resection of renal tumors was linked to a high risk of perioperative morbidity related to bleeding, surgeons started using renal embolization in the 1970s. In some individuals, transarterial embolization is a procedure that makes nephrectomy easier. Embolization reduces the need for transfusions, intraoperative blood loss, and operation time in patients with big or advanced renal tumors, which is advantageous in surgical resection. This implies that there are advantages to renal tumor embolization, such as lower tumor vascularity that enables early renal vessel ligation. The lymphoproliferative condition is increased by post-embolization tumor necrosis, and Natural Killer cells respond to the tumor specifically (4).

EVIDENCE ACQUISITION

A literature search was conducted using the PubMed, Embase, and Science Direct databases published between 2013-2023. Keywords used for searches included renal cancer, transarterial embolization, Amplatzer Vascular Plug and Gelatin Sponge Particles. This literature review examines the effectiveness of AVP and GSP in Transarterial Embolization of Kidney Tumors. Studies were assessed for quality and risk of bias, and data were extracted and analyzed.

EVIDENCE SYNTHESIS

The goal of vascular embolization is to interrupt blood flow or cause an inflammatory response in the vessel wall. Renal artery embolization has been used to treat a variety of renal conditions, ranging from symptomatic hematuria to palliative measures in malignant renal tumors. It is also commonly used in preoperative preparation for renal tumors, arteriovenous fistulas and other renal vascular malformations, post-biopsy com-

plications, and traumatic renal hemorrhage (5). Indications for embolization in the therapeutic management of neoplastic renal masses include palliative care for mass loss and bleeding risk in patients requiring total or partial nephrectomy or treatment with radiotherapy, as well as management hematuria and/or bleeding during and before and after trauma (6). Endovascular transcatheter embolization is considered the first-line therapy because of high success rate and shorter hospital stay. Compared to surgery, it has lower morbidity and mortality, which surgery is more invasive and has risk of intraoperative anesthesia. However, percutaneous embolization carries a significant migration risk of embolic material into the venous and pulmonary circulation (7,8).

Classification of embolic agents can be classified based on physical form (solid or liquid), mechanism of action (mechanical or chemical), and primary ingredients (biosynthesis, synthesis, etc.). However, most experts divide them based on the duration of the occlusion into temporary and permanent. Examples of temporary embolic agents are gelatin sponge, oxidized cellulose, and microfibrillar collagen. Meanwhile, permanent embolic agents include polyvinyl alcohol, tris-acryl gelatin microspheres, N-butyl cyanoacrylate, and plugs. Permanent embolic agents are considered modern embolic agents and are non-absorbable. The choice of embolic agent is based on the case to be treated, such as characteristic of renal fistula by size, location and flow rate, the desired duration of occlusion, the required tissue viability, and the patient's clinical condition. In the case of large blood vessels, the embolization type required is permanent embolization (8,9).

Coils are used most often because of their easy availability, low cost, and ease of use. However, they have a risk of migration into the venous and pulmonary circulation and generally require several spirals to completely occlude the vessel. Coils have been demonstrated to be less effective in embolization as the current preferred technique uses n-butyl cyanoacrylate glue which allows rapid and definitive distal occlusion of a voluminous vascular bed and causes necrosis in perivascular tissue (4). Plugs have entered clinical practice in recent decades, first for the treatment of heart diseases and then for the treatment of peripheral vessels. The Amplatzer Vascular Plug (AVP) is a recent innovation by St. Jude Medical. Its use as a peripheral embolic agent was approved by the United States Food and Drug Administration (FDA) in 2004, and was declared effective in a study published with year. The structure consists of nitinol-based braids that allow self-expansion across the target vascular bed. It can be repositioned and restored at any time after being released. The use of a 30 to 50 % larger device is crucial for achieving optimal blood vessel seal and preventing unintended peripheral embolism. AVP is a very effective, especially in cases related to the structure of the peripheral renal arteries. The structural characteristics of AVP IV allow for irregular and high-flow delivery into blood vessels and rapid targeted occlusion (5,8).

The use of AVP 2 has been widely reported and many have reported the success of use this device. AVP 2 is described in the embolization of renal AVFs in certain vascular territories, more specifically in high-flow renal AVFs. In several reported cases, the use of AVP 2 was found to be effective and safe. AVP 2 is more accurate and stable placement through a detachable system. It has a self-expanding, cylindrical occluding device made out of nitinol mesh wires. It can be safely used in short and high-flow vascular segments, such as renal AVFs, where coils are released with less precision and safety. After placement of the device, an angiogram can be performed to confirm placement and the device can then be deployed from the push wire in a deliberate, controllable and relatively precise by rotation pusher wire. Equipment can be removed and repositioned if the position is unsatisfactory, minimizing migration risks (7).

Several authors in many case reports recommend AVP 2 as the primary choice in cases of renal AVF occlusion with high-flow and short-vascular connection, where the occlusion has to be in an exact location. Its also to be more cost-effective compared to using coils. Compared with coils, the AVP 2 also has minimal metallic artifact features on computed tomography allowing for more accurate interpretation. The AVP 2 device is usually inserted using a sheath or guiding catheter which may be difficult if done in stenotic renal arteries or the distal part of the renal vessels because many fistulas are found in this area. In addition, the AVP 2 delivery cable is relatively stiff compared to the coil, allowing for difficulties in advancing the device in areas of tortuous blood vessel anatomy (7). Futhermore, re-

nal artery embolization in the preoperative setting can decrease perioperative blood loss, creation of a tissue plane of edema facilitating dissection, and reduction in tumor bulk including extent of vascular thrombus, when present. Wide variation in reporting markers such as reduction in intraoperative blood loss, transfusion requirements, surgical procedure time, surgical complications, and survival outcomes has limited its use to local practice patterns (11).

AVP IV can be placed in tortuous and small vessels resulting in complete occlusion of the target blood vessels in a short time. The use of a single device significantly reduces procedural time when positioning coils, in fact, more coils are often needed to completely occlude the blood vessel. The plug was released at the point of arteriovenous anastomosis without any involvement of non-target arteries. The technical characteristics of the device allow performing very precise preliminary examinations, ensuring selective occlusion of the target blood vessel segment with a very low risk of migration. The device's structural characteristics determine complete vessel occlusion within 10 minutes after release as it gradually adapts to the target vessel causing slowing down of the blood flow until it stops completely (8).

Apart from AVP, renal artery embolization can be carried out with embolic agents such as polyvinyl alcohol (PVA), n-butyl cyanoacrylate (NBCA), micro coils, and gelatin sponge particles (GSP). Embolic agents that are often used are NBCA and PVA as single agents or coils/PVA, GSP/PVA, and coils/GSP as combination agents. GSP is a very effective temporary embolic agent and has a fairly high clinical success rate (12). It is generally used in cases of bleeding, uterine fibroids, and hypervascularization in malignant tumors. It cause an uncontrolled level of occlusion because the instrument is cut by hand, resulting in particles that are difficult to calibrate and very easily deformed. GSP degradation is also said to last quite a long time, around 3 weeks to 4 months, and can be accompanied by a chronic inflammatory response (13).

The usage of GSP in transarterial embolization has increased as a result of its recognition as a potent agent for transitory arterial embolization. Within a few weeks after being embolized with GSP, the embolized arteries are recanalized, preserving normal tissue at the embolization site and enabling additional transarterial embolization to inhibit tumor growth. To achieve partial recanalization and complete thrombus, 4 weeks after embolization with GSP are required. However, the lumen of the recanalized artery has significant stenosis due to thrombus and intimal hyperplasia. This intimal hyperplasia is caused by the migration of smooth muscle cells from the media and collagen deposition. The massive organized thrombi and intimal hyperplasia due to mild embolization with GSP thus lead to arterial stenosis. The massive organized thrombosis appears to be caused by acute inflammatory reactions and foreign bodies, while intimal hyperplasia is due to arterial wall damage due to transmural inflammation and migration of smooth muscle cells after partial loss of continuity of the internal elastic lamina (14).

Several studies report the disadvantages of using GSP. Partial degradation of GSP also causes foreign body inflammation. This finding is to the existing theory that the occlusion caused by GSP is not total or not the same as its size but is smaller due to manual cutting techniques so that the inserted GSP instrument is roughly calibrated and can even change shape. Likewise, the finding by compared study showed that only 88 % of the occlusion was formed after 4 months of embolization, resulting in long-term incomplete recanalization. In this study, some GSPs will be degraded and recanalized around 80 % on day 7. These results may vary due to poor calibration. In another case, 63 % recanalization occurred on day 7 and 100 % on day 14 after embolization. Recanalization is accompanied by partial degradation of GSP and partial destruction and remodeling of the vessel wall with infiltration of inflammatory cells (13).

Tumors that received supplementary microcoil embolization had a significantly greater relative reduction in tumor volume at > 3 years after embolization. The differences in relative tumor reduction only became apparent at > 3 years after embolization suggests that using GSP without microcoil embolization reduced the long-term effects of embolization. Tumor feeders that are not occluded by additional microcoils can be recanalized more easily and quickly than occluded vessels, which may result in tumor regrowth. Indeed, in a representative case, renal arteriography showed revascularization of a tumor feeder that was not occluded by the microcoil during the original embolization (16) (Table I).

Table I. Summary table of literature search results

Authors	Study design	Summary of intervention	Summary of findings
Abdel-Aal *et al.*, 2014 (7)	Case report	A 68-year-old patient who had suffered from renal cell carcinoma. He had been treated with a partial nephrectomy and was found contrast with opacity in the renal vein which indicated an arteriovenal fistula and a pseudoaneurysm connecting the renal artery and vein at the site of previous partial nephrectomy. The patient was placed with an occlusion balloon catheter in the renal vein area close to the pseudoaneurysm to occlude the flow of the renal arteriovenal fistula and was then sent home after 24 hours of observation after the procedure	After 2 months, the renal arteriovenal fistula recanalized, so the patient underwent surgery again with the installation of a 6 mm AVP 2 in the area of the feeding artery branching and pseudoaneurysm. After observing at the 4th and 10th months after the procedure, no artifacts were found on the installed AVP 2 device, which means that no occlusion was found and there was also no evidence of re-canalization of the renal AVF, which indicates that this procedure was successful
Catelli *et al.*, 2020a (8)	Case report and literature review	A 57-year-old female patient was reported with nephrotic syndrome who had suffered for 10 years. About 5 years ago, a left kidney biopsy was performed which showed an intrarenal fistula that had caused clinical signs of heart failure in the last 2 years and worsened in the last 3 months. After further examination, the patient underwent surgery using a 6 Fr 45 cm introducer placed in the left main renal artery and a 7 × 12 mm AVP IV placed at the fistula site	After the procedure, the patient experienced post-embolization syndrome which was characterized by pain and fever, but during and after the procedure no complications were found. On 6 months after the procedure with CT scan angiography, no fistula was found with focal renal infarction < 20 % of the kidney volume. The patient's signs of heart failure decreased significantly so the treatment for this patient was considered successful
Catelli *et al.*, 2020b (10)	Case series	Three cases involving AVP installation in renal artery embolization	The patient's complaints were successfully handled without any complications during or after the procedure. Renal artery embolization with the use of AVP for the treatment of renal fistulas and neoplastic masses according to this case report shows excellent results without any complications

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Table I (cont.). Summary table of literature search results

Authors	Study design	Summary of intervention	Summary of findings
Karundeng *et al.*, 2023 (6)	Case series and literature review	5 renal arterial embolization cases with AVP, 3 patients had right renal tumors and 2 patients had left renal tumors	Preoperative renal artery embolization is a safe procedure with a relatively low complication rate. Preoperative renal artery embolization appears to be a useful tool in the surgical management of large masses and advanced disease
Sukamto *et al.*, 2022 (5)	Case Series	3 cases of patients with left renal cell carcinoma who underwent renal artery embolization with AVP. The goal of intervention in their case was to maximize blood flow obstruction. In the first case, the main artery was occluded with AVP while the smaller accessory artery was occluded with Gel Foam, resulting in complete occlusion. The same method was used in their third case, with the accessory artery embolized with a mixture of ns-PVA and Gel Foam. Both cases achieved complete embolization and successful nephrectomy with minimal intraoperative bleeding. In the second case, the size of the artery was 8 mm and the AVP was 50 % larger, 12 mm in diameter, deployed accurately with good positioning. Blood flow decreased significantly after 15 minutes of assessment but was not obstructed. They decided not to wait the additional fifteen minutes (to assess the degree of obstruction) as recommended because the patient was so agitated that it was necessary to complete the procedure. However, the nephrectomy over the next 24 hours was successful	AVP embolization of the main renal artery, ns-PVA and Gel-foam combination for embolization of the accessory renal artery provide good surgical results and also cost-effective
Oh *et al.*, 2015 (14)	Experimental	The experimental study using rabbit cells, aggregates of macrophages and polymorphonuclear leukocytes occurred in the lumen of blood vessels containing GSP. GSPs were mostly located in the renal segmental and interlobar arteries, causing proximal occlusion	On 1 week after embolization, focal intimal destruction occurred accompanied by transmural inflammation of the arterial wall. In the intimal tunica, many inflammatory cells were found in the form of polymorphonuclear leukocytes, in the medial tunica and adventitia there was thickening with the proliferation of smooth muscle cells. However, 1 week after embolization, total occlusion was found in the embolized artery. After 2 weeks, partial resorption of GSP occurred, and an inflammatory reaction due to the presence of a foreign body in the form of GSP. This inflammatory response will decrease within 4 weeks after embolization

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Table I (cont.). Summary table of literature search results

Authors	Study design	Summary of intervention	Summary of findings
Chen *et al.*, 2021 (12)	Case series	18 patients with Acquired Cystic Kidney Disease (ACKD), 5 of them were given GSP embolic agent therapy, of which 4 were combined with other embolic agents and 1 used GSP alone	Five cases has been succesfull both technically and clinically. Various embolic agents, alone or a combination of embolic agents, were very effective in hemostasis. Except for one case where GSP alone was used, permanent embolic agents were used, and it appears to have contributed to high clinical success. However, the case that given GSP agent alone experienced complications in the form of post-embolization syndrome which was characterized by mild abdominal pain, fever, leukocytosis, and an increase in C-reactive protein within 24 hours after embolization this can be managed quickly
Gong *et al.*, 2021 (15)	Case series	22 patients with Wunderlich Syndrome (WS) when it leads to hypovolemic shock due to a ruptured renal angiomyolipoma (rAML), who underwent urgent transcatheter arterial embolization. Different embolic materials are selectively used based on the decisions of interventional radiologists. From 6 of them used the embolic agent GSP alone (4 patients) and GSP in combination with micro coils (2 patients)	Six patients experienced embolic success both technically and clinically. During a median follow-up of 34 months, no recurrent hemorrhage requiring repeat endovascular or surgical treatment occurred. Urgent transcatheter arterial embolization with selective use of different embolic materials effectively control WS with hypovolemic shock secondary to ruptured rAML. However, in this study, it was not explained in detail regarding the success achieved after using GSP
Maeda *et al.*, 2013 (13)	Experimental	They using pig renal arteries for embolization	Their found that GSP was still visible on imaging at the proximal and distal levels on 7th day

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Table I (cont.). Summary table of literature search results

Authors	Study design	Summary of intervention	Summary of findings
Zhang *et al.*, 2023 (16)	Case series	They examined the effect of supplementary microcoil embolization on the long-term progression of renal angiomyolipoma (rAML) embolized using GSP in 29 unruptured rAML patients. 11 patients received microcoil embolization and 18 patients did not	None of them had post-embolization hemorrhage, underwent surgery, or recurrence of aneurysms ≥ 5 mm. All patients experienced post-embolism syndrome consisting of fever, pain, vomiting or nausea, which was relieved by medication. No patients experienced other complications related to the procedure. There were no significant differences between two groups in the distribution of comorbidities, original tumor volume, percentage of fat content before embolization, or relative reduction in tumor volume

CONCLUSION

In several case reports, the use of AVP is effective and safe on transarterial embolization procedure for renal tumors. AVP is very effective in use, especially in cases associated with peripheral renal artery structures. Using GSP requires a long time and recanalization. To achieve partial recanalization and complete thrombus, 4 weeks post-embolization with GSP is required.

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