Korean J Neurotrauma. 2022 Oct;18(2):178-187
https://doi.org/10.13004/kjnt.2022.18.e37
pISSN 2234-8999·eISSN 2288-2243

KJNT

Review Article

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Role of Transarterial Embolization in the Treatment of Life-Threatening Hemorrhage in Patients With Maxillofacial Injury

Junhyung Kim, Sang Kyu Park, and Joonho Chung

Department of Neurosurgery, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

OPEN ACCESS

Received: Apr 27, 2022
Revised: Jul 11, 2022
Accepted: Jul 23, 2022
Published online: Aug 31, 2022

Address for correspondence:
Joonho Chung
Department of Neurosurgery, Gangnam Severance Hospital, Yonsei University College of Medicine, 20 Eonju-ro 63-gil, Gangnam-gu, Seoul 06229, Korea.
Email: ns.joonho.chung@gmail.com

ORCID iDs
Junhyung Kim
https://orcid.org/0000-0002-8908-978X
Sang Kyu Park
https://orcid.org/0000-0001-9231-0716
Joonho Chung
https://orcid.org/0000-0003-2745-446X

Presentation
A part of the contents in this manuscript was presented in the 5th Neurotrauma Focus meeting held by Korean Neurotraumatology Society in January 2022.

Conflict of Interest
The authors have no financial conflicts of interest.

ABSTRACT

Life-threatening hemorrhage following maxillofacial injury (MFI) is rare but can be fatal. Conventional measures for hemostasis including nasal packing, balloon tamponade, and surgical ligation of bleeding points may not be effective or efficient in patients at risk of hypovolemic shock. Advantages of transarterial embolization (TAE) include rapid identification of the bleeding focus and its access, direct obstruction of the culprit vessels, ability to control multiple bleeding sites, and no requirement of general anesthesia. The internal maxillary artery is the most frequently targeted vessel for embolization. Several studies have demonstrated that TAE was technically successful at rates between 79.4% and 100% and was associated with good clinical outcomes. However, major complications such as tongue necrosis or facial nerve palsy have rarely been reported (0%–7%), probably because of rich collaterals in the maxillofacial region, and failure to diagnose complications in patients who are severely disabled or died. Traditionally, Gelfoam and coils have been widely used as embolic materials. Polyvinyl alcohol particles and n-butyl-cyanoacrylate are also favored, and newer embolic materials, such as Onyx or precipitating hydrophobic injectable liquid, are available for use. Operators should be familiar with the distinctive characteristics of each embolic material. Early treatment with TAE for intractable hemorrhage may improve outcomes in patients with MFI, and further studies are necessary to develop a treatment algorithm to define when to initiate TAE in cases of severe oronasal hemorrhage following MFI.

Keywords: Carotid artery injury; Embolotherapy; Endovascular procedures; Multiple trauma; Hemorrhage

INTRODUCTION

Maxillofacial injury (MFI) is a common and rarely fatal condition in trauma patients, with prevalence ranging from 17% to 69%.[38] It is usually caused by blunt facial trauma due to traffic accident, assault, fall, or suicidal attempts.[5] However, in severe cases of maxillofacial injury, the initial resuscitation process comprising the airway, breathing, and circulation management is crucial for patient survival.[8,10,27] Primary medical attention must be administered to protect the airway and maintain stable respiration, as airway maintenance can be complicated by excessive oronasal bleeding, soft-tissue swelling in the nasopharynx, decreased level of consciousness, and vomiting.[15,29] Airway protection may require invasive procedures such as endotracheal intubation, cricothyroidotomy, and tracheostomy, as the soft tissues of the lower face can obstruct the pharynx.[20] Hemorrhage is a significant cause of mortality in patients with MFI.[37] Patients with MFI are susceptible to the development of massive hemorrhage due to the rich arterial supply to the head and neck region. Life-threatening hemorrhage occurs in 1.0% to 4.5% of patients with MFI, and failure to control bleeding can result in mortality rates as high as 85.9%.[1,4,14,24,36] The purposes of hemostasis in patients with MFI include the restoration of systemic hemodynamic stability and protection of the airway from the pooled blood in the oropharynx that can obstruct the airway and cause vomiting.[15]

Conventional measures to control bleeding include nasal packing, balloon tamponade, surgical ligation of the bleeding point, coagulopathy reversal, and internal maxillary fixation.[1,2,16] However, compression by nasal packing or balloon tamponade is often ineffective, especially when the deep arteries are responsible for bleeding, since the surrounding structure in the midface consists of insufficient solid bones to compress against.[1,18,36] Cogbill et al.[8] reported that this technique was successful in only 29% of patients with severe oronasal hemorrhage. Surgical ligation of the external cerebral artery (ECA) is a definitive treatment option but can be challenged by the swelling of soft tissues or defects of the neck and face, as well as the complex anatomy of the maxillofacial region.[27] Furthermore, it often requires bilateral neck exploration, causing an increased risk of morbidity and mortality.[4]

Transarterial embolization (TAE) has become a favored treatment option in maxillofacial trauma management as it offers several advantages over conventional hemostasis methods. For example, an operator can identify bleeding points more clearly, overcome the deep and complex anatomy of injured areas, and directly occlude multiple culprit vessels in a short period of time.[2,17,22,24,27] Moreover, TAE has been widely performed to treat massive pelvic bleeding or retroperitoneal bleeding, which is frequently observed in patients with severe MFI.[7,25] However, studies that describe TAE for hemostasis of severe MFI are often limited by a small number of cases and heterogeneity in the indications for the procedure. This article aimed to review and discuss the literature on the management of MFI with life-threatening hemorrhage and the role of TAE for hemostasis to help readers understand the indications for the procedure and its technical considerations.

COMMON BLEEDING VESSELS IN MFI WITH INTRACTABLE HEMORRHAGE

The internal maxillary artery (IMA) is the most common vessel responsible for intractable hemorrhage. In a study of 32 MFI patients treated with TAE, Cogbill et al.[8] reported that the IMA was most often embolized (65%), followed by the facial artery (13%), internal carotid artery (ICA) (4%), and lingual artery (4%). Kuan et al.[19] presented a similar distribution of the site of injury in a study of TAE treatments of 26 patients with traumatic MFI, with IMA being the most common bleeding vessel (31.6%), followed by other ECA branches, such as the facial artery (15.9%) and lingual artery (15.9%). Another study found that all 12 cases of intractable oronasal hemorrhage occurred from the pterygomaxillary part of the IMA.[22] It should also be noted that the branches of the ICA, such as the ethmoid branches of the ophthalmic artery are major blood suppliers to the midface region.[36]

https://doi.org/10.13004/kjnt.2022.18.e37

INDICATIONS FOR TAE SUGGESTED BY PREVIOUS STUDIES

TAE of the ECA is considered in life-threatening hemorrhage situations when less invasive procedures fail to stop active bleeding, which occurs at reported rates ranging from 21% to 53%.[8,33] However, the criteria for failure of conservative treatments may vary. Bynoe et al.[4] proposed a management algorithm for life-threatening hemorrhage in MFI and suggested that TAE should be performed when local measures such as compression, packing, and direct cauterization fail to control the hemorrhage, and that hemodynamic compromise persists with continuous blood product replacement. Another group performed TAE in trauma patients when fluid resuscitation with 2 L in 15 to 20 minutes resulted in only a transient response.[13] Chen et al.[6] suggested a guideline for the management of life-threatening hemorrhage in MFI and argued that diagnostic angiography and TAE should be performed when blood product replacement exceed 1,500 mL and systolic blood pressure (SBP) is <90 mmHg, or bleeding resumed immediately after nasal unpacking. The authors claimed that their lower cut-off for the resuscitation volume would lead to sooner hemodynamic stabilization and avoidance of the side effects of massive transfusion such as disseminated intravascular coagulation.

Typical angiographic findings encountered in patients with intractable hemorrhage are contrast extravasation from the culprit vessels (**FIGURE 1**) or the presence of pseudoaneurysms. Active bleeding may not be obvious in angiography in some cases, but TAE of suspected ECA branches can often achieve successful hemostasis.[12]

CLINICAL OUTCOMES OF TAE IN PATIENTS WITH MFI WITH LIFE-THREATENING HEMORRHAGE

Data from several studies or case series pertaining to the TAE treatment of life-threatening hemorrhage in patients with MFI are summarized in TABLE 1. Various studies and case reports have demonstrated the high efficacy of TAE in controlling intractable bleeding associated with MFI, with technical success rates ranging between 79.4% and 100%. Lee et al.[23] reported about 12 patients with maxillofacial fractures with oronasal bleeding intractable to non-invasive hemostatic procedures treated by TAE of the ECA.[22] TAE was successful in all patients, and no procedure-related complications were noted. A similar study by Liao et al.[23] revealed 79.4% successful hemostasis achieved by TAE. Bilateral hemorrhaging arteries were observed in 26.5% of the patients. In a series reported by Cogbill et al.,[8] bilateral TAE was performed in approximately 35% (11/32) of patients with intractable oronasal bleeding to achieve a definite hemorrhage control rate of 87.5%.

Procedure-related complications of TAE may include blindness, facial nerve palsy, vascular injury, tongue necrosis, and embolic ischemia, but they have rarely been reported.[4,18,20,34] In a study of 11 patients with MFI with intractable hemorrhage treated with TAE, Bynoe et al.[4] experienced 1 patient with partial tongue necrosis from bilateral ECA embolization and one patient with facial nerve palsy from left IMA embolization. The authors suggested that TAE should be performed above the lingual artery to avoid tongue necrosis. Chen et al.[6] reported two major complications directly related to TAE in 28 patients (7% complication rate), including one facial nerve palsy and one partial tongue necrosis. The tongue necrosis occurred in a patient who received bilateral ECA embolization below the lingual artery. Several other studies or case reports regarding TAE of intractable hemorrhage due to

https://doi.org/10.13004/kjnt.2022.18.e37

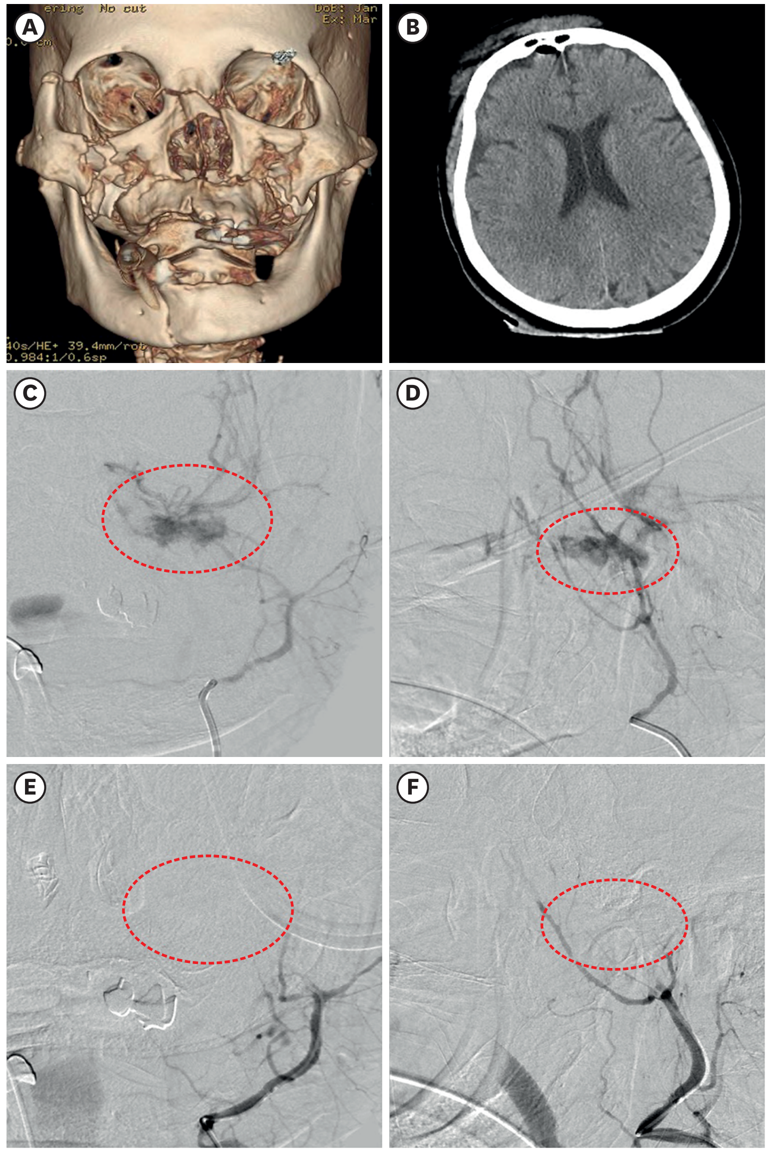

FIGURE 1. A 77-year-old female was transferred to our institution with decreased consciousness, active oronasal bleeding, multiple facial laceration and facial deformity after a fall from 5 meters high. (A) 3D reconstruction image of facial CT and (B) brain CT showed multiple facial bone fractures and pneumocephalus without traumatic intracranial hemorrhage. (C) AP and (D) lateral views of selective angiography of left ECAs showed contrast extravasation in the distal branches of the IMA. After embolization of the left IMA with PVA particles (a range of particle size, 250–350 microns), (E) AP and (F) lateral view of the left ECA angiography demonstrated disappearance of the extravasation in the distal branches of the left IMA. Red-dot circles indicate the extravasation and disappearance of the extravasation.
CT: computed tomography, AP: anterior-posterior, ECA: external cerebral artery, IMA: internal maxillary artery, PVA: polyvinyl alcohol.

MFI reported 0% major complication rate.[18,19,22,23] One of the reasons for the low major complication rate is the rich collateral arterial network between the bilateral ECA branches in the midface.[3,4] Another possible reason is the underdiagnosis of procedure-related complications in patients who died or became vegetative after severe MFI.[6] Perhaps, more accurate estimates of the procedure-related complications of TAE for hemostasis of MFI would be the complication rates reported by the studies with intractable epistaxis, which were between 2% and 4%.[9,11,39] However, it should be noted that advances in endovascular

TABLE 1. Summary of previous studies or cases series on TAE in the treatment of life-threatening hemorrhage following MFI

Authors	Year	Number of cases	Embolized vessels	Embolic materials	Technical success*	Complications	Factors associated with good prognosis
Bynoe et al.[4]	2003	11	IMA: 5, ECA: 6	Gelfoam, Coil, PVA	100%	Tongue necrosis: 1, Groin hematoma: 2, Facial nerve palsy: 1	Not analyzed
Liao et al.[22]	2007	34	IMA: 25, MMA: 5, Sphenopalatine artery: 4, STA: 4 ECA: 4, Others: 4	Not specified	79.4% (combined with nasal packing)	None	Higher GCS score, Lower shock index, Lower injury severity score
Cogbill et al.[8]	2008	32	IMA: 33, FA: 7, ICA: 3, ECA: 2, LA: 2, Others: 4	Microcoil with or without Gelfoam	87.5%	None	Not analyzed
Chen et al.[6]	2009	8	IMA: 7, STA: 1, ECA: 1	Gelfoam, Microcoil & Gelfoam	100%	None	Not analyzed
Kuan et al.[18]	2015	26	IMA: 12, FA: 6, LA: 6, MMA: 5, ECA: 3, Others: 6	Gelfoam, PVA, Microcoil, NBCA	92.3%	None	Higher GCS, Lower injury severity score, Initial hemoglobin >10 g/dL, Brain midline shift
Lee at el.[21]	2016	12	IMA: 12	PVA	100%	None	Initial GCS, Lowest SBP, Less transfusion, Less time to TAE

TAE: transarterial embolization, MFI: maxillofacial injury, IMA: internal maxillary artery, ECA: external carotid artery, PVA: polyvinyl alcohol, MMA: middle meningeal artery, STA: superficial temporal artery, GCS: Glasgow Coma Scale, FA: facial artery, ICA: internal carotid artery, LA: lingual artery, NBCA: n-butyl cyanoacrylate.
*Complete hemostasis achieved after successful TAE.

devices, such as microcatheters and wires, have led to a decrease in the complication rates in more recent studies.[11,21,34)]

A few studies have evaluated the prognostic factors associated with TAE treatment in patients with MFI. In a study comparing the clinical outcomes of TAE and non-TAE treatments for life-threatening hemorrhage with MFI defined as blood loss of >20%, the authors demonstrated that TAE was an independent predictor for better outcomes, and hypotension (SBP <90 mmHg) and a low Glasgow Coma Scale score of ≤8 were associated with mortality.[27)] Similarly, Liao et al.[23)] revealed that successful TAE hemostasis was strongly associated patient survival. Lee et al.[22)] demonstrated that the number of blood product replacements and the time from arrival to groin puncture were negatively correlated with good clinical outcomes. In their study, the mean values for the lowest SBP and red blood cell transfusion were 62±6.4 mmHg and 15.3±4.3 units, respectively. Lower shock index (heart rate/SBP) before and after TAE was associated with a better outcome, and TAE significantly improved the shock index.[14,23)]

Decreased mental status or brain injury at the time of treatment is associated with poor outcomes.[8,19,22,23)] In patients with traumatic brain injury (TBI) who require craniotomy operations, whether TAE should precede cranial operation remains controversial.[42)] In our opinion, hemodynamic stability should be achieved to ensure a safe operation such as craniotomy.

The results of the aforementioned studies imply that the early initiation of TAE hemostasis in patients with intractable hemorrhage due to MFI may be associated with better clinical outcomes by preventing hypovolemic shock with fewer blood product replacements. Wong at al.[42)] argued that early treatment with TAE in the pre-shock state might decrease the amount of blood transfusion and improve the outcome, although it would be difficult to move a severely injured, hemodynamically unstable patient for diagnostic angiography.

https://doi.org/10.13004/kjnt.2022.18.e37

EMBOLIC MATERIALS

Several embolic materials with inherent properties and characteristics can be used in embolization therapy. An operator can choose embolic materials based on clinical factors such as target vessel caliber, type and severity of vessel injury, familiarity with the materials, and whether or not to occlude the target vessel permanently.

Gelfoam (Pfizer, Kalamazoo, MI, USA) and coils are well-known embolic materials that have been used for several decades.[20,31] Gelfoam is a sponge-like material with hemostatic properties made from porcine skin gelatin. Small pieces of Gelfoam can be mixed with a contrast solution and injected via the catheter for temporary occlusion of the target vessel by inducing a foreign body reaction, resulting in thrombus formation.[35] Gelfoam is suitable for vessels with large calibers that do not need to be permanently occluded. It is thought that recanalization occurs within 3 weeks to 3 months, but in many cases, temporary embolization can effectively control the bleeding.[26,31] Drawbacks of embolization using Gelfoam include the unpredictability of the procedure due to the inconsistency of sizes and amounts of Gelfoam pieces, and the potential risk of aerobic infection provided by air bubbles formed in the Gelfoam-contrast mixture.[40]

Coils of various lengths, shapes, and stiffness are available. It occludes vessels by providing mechanical obstruction with its mass and delayed thrombosis formation within the coil mass. Dense packing with coils can slow arterial flow, but is sometimes insufficient to achieve immediate and complete hemostasis in larger vessels. Furthermore, decreased clotting factors in the circulation may prolong thrombus formation in patients with severe bleeding.[26] In such cases, the Gelfoam-coil sandwich can be utilized to achieve fast and permanent embolization.[26] Possible complications of using coil embolization include vessel injury, coil migration, and non-target vessel occlusion.[40]

Polyvinyl alcohol (PVA) particles (Boston Scientific, Cork, Ireland and Cordis J&J Endovascular, Miami, FL, USA) are permanent embolic materials with diameters between 100 and 1,100 μm. They provide permanent occlusion by adhering to the vessel walls, causing flow stagnation, or occluding small vessels that they fit in.[30] Advantages of PVA particles are simple embolization techniques and immediate occlusion of target vessels. However, due to the method of preparation, PVA particles can be irregular in size such that particles smaller than the stated size range can be included, which may cause undesired distal vessel occlusion.[31,40] Moreover, owing to their adhesive property, catheter occlusion or a premature occlusion of the proximal artery may occur.[40]

N-butyl cyanoacrylate (NBCA) (TruFill®; Cordis, Miami Lakes, FL, USA and Histoacryl®; B. Braun Aesculap, Tokyo, Japan) is a synthetic liquid embolic agent. It should be mixed with tantalum powder, a radiographic opacifier, and ethiodized oil, a polymerization retardant. Once the NBCA glue mixture is exposed to an anionic environment, such as blood, it rapidly polymerizes to form a permanent cast inside the vessel. The concentration of NBCA determines the rate of polymerization and ease of penetration.[20] It offers a few advantages in the setting of major trauma: 1) embolization does not depend on the inherent clotting factors; and 2) it can be prepared quickly and provides selective, immediate occlusion of a target vessel.[31] A disadvantage of NBCA glue embolization is that it requires a skilled operator to precisely control its polymerization rate.

Onyx (Medtronic, Dublin, Ireland) and precipitating hydrophobic injectable liquid (MicroVention, Tustin, CA, USA) are newer liquid embolic materials that are available. Although these liquid embolic materials have strengths, their use in the TAE of bleeding vessels in intractable hemorrhage has rarely been reported.

CLINICAL CONSIDERATIONS IN THE MANAGEMENT OF LIFE-THREATENING ORONASAL BLEEDING IN PATIENTS WITH MFI AND WHEN TO PROCEED WITH TAE

Based on previous literature regarding trauma management and our experiences, we suggest considering the following aspects when treating patients with oronasal bleeding due to severe MFI.

Airway and breathing

Securing the airway and maintaining stable breathing are the foremost goals. This may require proper positioning of the patients or invasive procedures, such as endotracheal intubation or cricothyroidotomy. Special attention should be given to stabilization of the cervical spine, as the incidence of cervical spine injury associated with MFI can be as high as 8%.[28]

Circulation

When hemodynamic instability is observed, nasal packing and fluid resuscitation with crystalloids and blood products are performed. Computed tomography of the other organ systems is recommended for the identification of co-injuries in hemodynamically stable patients. In blunt trauma without TBI, SBP of 80–90 mmHg is permitted, but in patients with TBI, SBP >90 mmHg or mean arterial pressure >80 mmHg should be aimed at maintaining cerebral perfusion.[41] The European guidelines on the management of major bleeding and coagulopathy following trauma suggest a restricted volume replacement to achieve the target blood pressure until bleeding is controlled.[32] Therefore, we recommend an immediate transition to TAE in the following situations:

- Active arterial bleeding persists in the oronasal cavity after nasal packing
- Target SBP of 90 mmHg was not achieved within 60 minutes of resuscitation or with 1,500 mL of fluid, including blood product replacement.
- TBI or bleeding from the pelvic cavity or intra-abdominal organs is confirmed or highly suspected.

Diagnostic angiography and TAE

Transfemoral access should be the first option since TAE of possible bleeders in the abdominopelvic cavity may be necessary. Bilateral ECA and ICA angiography should be performed to identify the culprit vessels and dangerous ECA-ICA anastomoses. In our experience, nasal packing or manual compression often disguised a sign of bleeding (contrast extravasation) on angiography; thus, when contrast extravasation is not well recognized, temporary removal of compression of the oronasal cavity can be considered. PVA with various particle sizes is available for the embolization of distal branches with a relatively small caliber. When proximal ECA branches with larger calibers should be occluded, coils combined with Gelfoam can be useful. An illustrative case is presented in **FIGURE 1**.

https://doi.org/10.13004/kjnt.2022.18.e37

CONCLUSION

TAE can be an efficient treatment option in patients with intractable hemorrhage due to severe MFI. It allows for localization of the culprit vessels, rapid access to surgically inaccessible vessels, and direct control of the origin of bleeding without requiring general anesthesia. Previous studies have indicated that earlier TAE controls bleeding and improves clinical outcomes. Development of a goal-directed treatment algorithm for patients with MFI at risk of hypovolemic shock and a well-trained multidisciplinary team are needed to achieve improved treatment outcomes for these patients.

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