Balloon-assisted injection of fibrin sealant for the treatment of postintervention access-site bleeding complications

Jakob U. Lindner MD | Matthias Markuske MD | Lukasz Szczanowicz MD | Alexander Jobs MD | Mohamed Abdel-Wahab MD | Steffen Desch MD | Holger Thiele MD | Dmitry S. Sulimov MD

Abstract

This study sought to evaluate a new method that uses injection of fibrin sealant under simultaneous balloon occlusion for the treatment of postinterventional access site bleeding complications. With the rising complexity of interventional procedures, iatrogenic false aneurysms and active bleeding has become more common. In general, these complications are associated with increased morbidity and mortality, especially if surgical repair is required. Although high success rates are reported for ultrasound-guided compression and ultrasound-guided thrombin injection, these methods are not always feasible. All procedures of fibrin sealant injection under simultaneous balloon occlusion for the treatment of postinterventional access site bleeding complications or pseudoaneurysm were prospectively collected. Additional data were retrospectively obtained and analyzed for all patients treated by this new method. In total, 53 patients were included from 2018 to 2021. Most of the access site complications were related to transcatheter aortic valve replacement (40%) or percutaneous coronary intervention (21%), but also to a wide variety of other procedures. Of the 53 patients, 30 had to be treated for false aneurysms and 23 for active bleeding. A high primary success rate of 94% was achieved. Recurrences of false aneurysms occurred in six patients, of which only one needed open surgical repair. Regarding complications, two peripheral embolisms, thereof one requiring additional stent implantation occurred. Balloon-assisted thrombin injection seems to be feasible and safe. It provides a new alternative to prevent surgery for patients where common techniques are unavailable or have failed.

Keywords

bleeding complications, peripheral complications, pseudoaneurysm, vascular access
1 | INTRODUCTION

Access site complications remain a relevant limitation of interventional procedures and are associated with increased morbidity and mortality. Although improvements have been made over the years, predominantly due to increasing experience, preferred radial over femoral access and advancements in vascular closure device (VCD) design and application, the increasing number of transcatheter aortic valve replacement (TAVR), and complex coronary interventions leads to an aggregate number of access site and bleeding complications that often require treatment. Life-threatening bleeding and major vascular complications after TAVR occur in up to 15.6% of cases, and false aneurysms/pseudoaneurysms (PSA) after coronary interventions are reported at a rate between 0.7% and 6.25%.

The most common first-line treatment of PSA is ultrasound-guided compression therapy (UGCT), which has a variable reported success rate of 54%–100%. The limitations of this method include pain, patient discomfort, time requirements, prolonged immobilization, the potential for thrombosis of femoral vessels, and decreased success due to periprocedural anticoagulation, the complex anatomy of the PSA, or large wall defect. Alternative techniques after failed UGCT include ultrasound-guided thrombin injection (UGTI), where certain sac and neck characteristics of the PSA need to be met, or surgical treatment. Surgical PSA repair should only be reserved for cases where other procedures are not feasible, as the complication rate of surgery is reported from 20% up to 71%, including bleeding, infection, neuralgia, prolonged hospital stay, perioperative myocardial infarction, and death.

Regarding major access-site bleeding after TAVR, which is commonly due to VCD failure, the treatment options are limited. In addition to the surgical approach, the interventional implantation of a covered stent is a common technique. A major drawback of this method, apart from its periprocedural risks, is the introduction of foreign material in an otherwise mostly healthy blood vessel, with risks of stent fracture, thrombosis, and stenosis.

To circumvent the abovementioned issues with the common methods for treatment of access-site bleeding, we recently described a new technique using TISSEEL fibrin sealant (Baxter International) injection during simultaneous balloon occlusion. The goal of this study was to evaluate the success rate of this technique and identify relevant complications after gathering experience with this method over a three years period.

2 | MATERIALS AND METHODS

Between July 2018 and March 2021, all procedures of fibrin sealant injection under simultaneous balloon occlusion for the treatment of postinterventional access site bleeding complications or PSA performed at the Heart Center Leipzig, Germany, were prospectively collected. Additional data were retrospectively obtained and analyzed for all patients treated by this new method.

2.1 | Patient selection

For cases with active bleeding, only patients with noncompressible bleeding or failed manual compression (at least 30 min of compression) were treated with the balloon-assisted TISSEEL injection (BATI) technique.

Regarding patients with PSA, the decision of whether to proceed with ultrasound-guided treatment or using angiography guidance was left to two physicians with experience in both techniques (M. M., D. S.). Large-bore vascular access, short and wide neck of the aneurysm, difficult visualization with ultrasound, and high retrograde flow with risk of embolization of the native artery were criteria for BATI.

2.2 | Procedure

The technique of BATI has previously been described by our group by Sulimov et al. Depending on the available vascular access sites, patient’s length and diameter of the target vessel, a contralateral femoral access or radial/distal radial access was used.

After obtaining the arterial vascular access in the conventional manner, the target artery was engaged with a catheter and wired. An angiogram of the affected artery was performed to determine the exact location of the bleeding and understand the specific anatomy (Figure 1A).

A 1:1 sized balloon catheter was then placed into the target artery exactly at the orifice of the arterial wall defect to completely occlude the bleeding source (Figure 1B).

The bleeding channel or PSA was then punctured with an 18 G needle under fluoroscopic or ultrasound guidance, during a short period of balloon deflation to visualize the bleeding source. The position of the needle within the bleeding channel was confirmed with an angiogram, direct needle contrast injection, and active bleeding through the needle while the balloon was deflated (Figure 1C). The balloon was then reinflated, and complete occlusion of the affected vessel was confirmed with angiography or ultrasound. TISSEEL fibrin sealant was then injected into the channel. After 30 s the balloon was removed, and the result was confirmed by angiography (Figure 1D).

In case of residual flow within the aneurysm, additional balloon inflation for 1–3 min or additional injection of the fibrin sealant was performed. Figure 2 shows the treatment of a large PSA with neck size of approximately 6 mm.

All patients underwent postprocedural ultrasound to ensure complete thrombosis of the bleeding and to exclude any further vascular complications at 24–48 h after the index procedure.

2.3 | Endpoints

All BATI procedures were prospectively entered into a database. After approval from the ethics committee of the University of Leipzig, additional relevant data were obtained retrospectively from the clinical database of the Heart Center Leipzig at the University of
Leipzig, including procedural-/clinical data, postinterventional in-hospital follow-up, and imaging. The primary endpoints were the ability to achieve hemostasis at the end of the procedure and recurrence of bleeding/PSA. Secondary endpoints were complications like peripheral embolism, infection, and relevant bleeding of the new access site.

2.4 | Statistical analysis

Continuous variables are shown as the median and interquartile range (i.e., 25th and 75th percentile). Categorical variables are shown as absolute numbers and frequency. In addition to descriptive statistics, univariable logistic regression models were formulated to study the association of presumed risk factors with the primary and secondary endpoints. The following presumed risk factors were selected according to clinical expertise: age, body mass index, sheath size of the initial procedure, diabetes, and clinically relevant peripheral artery disease (symptomatic or previous invasive treatment). $p$ values were judged as significant if less than 0.05. The statistical analysis was performed using R version 4.0.3 (R Foundation for Statistical Computing).

3 | RESULTS

In total, 53 patients were treated with the BATI method from July 2018 until March 2021. The group was relatively heterogeneous with the youngest patient being 12 and the oldest being 93 years old (median 77). TAVR (40%) and left heart catheterization/percutaneous coronary intervention (21%) were the most common causes for the access site complication, but the population also included patients after catheter ablation, extracorporeal membrane oxygenation (ECMO)/impella insertion, peripheral percutaneous transluminal angioplasty, transcatheter mitral edge-to-edge repair, renal denervation, left atrial appendage closure, and pediatric cardiac intervention. The detailed patient characteristics, including antiplatelet/anticoagulation therapy, sheath size, and VCD usage are displayed in Table 1.

Of the 53 patients, 30 patients had to be treated with BATI for PSA and 23 for active bleeding. The most common target vessels were the common femoral artery (45%) and the superficial femoral artery (40%). The usual new vascular access to reach the target area was the contralateral common femoral artery or the distal radial artery (“snuffbox”) with 66% and 25%, respectively. The procedural data are displayed in Table 2. The procedure duration times were calculated from the first to the last angiogram as these were the most accurate documented values. The time, therefore, does not include patient preparation, as well as obtaining and closure of the new vascular access. The median duration time was 27 min, with no relevant differences between the PSA and active bleeding group. Procedural duration times varied widely, depending mostly on the complexity of the procedure. The shortest (7 min) was observed in a PSA case with simple anatomy and the longest (90 min) was required for the treatment of a huge chronic PSA, where a very large amount of the sealant was needed to close the aneurysm.

The summarized outcome is displayed in Table 3. Primary success rates in the PSA and active bleeding groups were 93% and 96%, respectively (combined 94%). Only a partial thrombosis was achieved in the two primary failed PSA cases, but complete thrombosis was ensured after additional UGTI. Regarding the active bleeding group, one primary closure failed due to TISSEEL injection adjacent to the bleeding channel, which led to significant compression, but not total occlusion. Complete thrombosis could again be achieved after additional UGTI the following day.

Recurrence rates after primary successful closure were 14% (four patients) and 9% (two patients) for the PSA and active bleeding groups, respectively (combined 12%). Two patients in the PSA group were successfully treated with UGTI, one required the implantation of a percutaneous transluminal angioplasty.
of a covered stent and one underwent open surgical repair. The
decision for surgery was also made in part due to an additional
arterio-venous fistula and a high risk of venous thrombosis or em-
bolism during additional injections of thrombin/fibrin. The two pa-
tients in the active bleeding group developed a PSA before discharge,
but no major/life-threatening bleeding occurred. One of the patients
was successfully treated with prolonged manual compression and
one with additional UGTI.

Regarding complications, two cases with peripheral embolism
were observed. One of these occurred in a case where the superficial
femoral artery had to be recanalized in the same session, due to a
dislocated MANTA® device. A thrombus in the superficial femoral
artery was detected in the control angiography after TISSEEL injec-
tion and was successfully treated with additional stent implantation.
In the second case of peripheral embolism, a small thrombus in a side
branch of the deep femoral artery was detected, which required no
further treatment. No other adverse events occurred due to this
method, including infection or new access site complications.

No statistically significant risk factors were found for the failure
of primary closure, recurrence, or peripheral embolism in logistic
regression analysis (Table 4). Regression analysis of peripheral artery
disease regarding influence on primary closure success was not
performed, as the low number of events and rare occurrence of
peripheral artery disease would have led to invalid results.

This observational single-center study showed that BATI treatment of complicated PSA or active bleeding is possible with a high success and low complication rate. We could not find any predictors of success or failure of BATI based on anatomic or patient-specific criteria.

In general, the significance of access site complications in interventional procedures should not be underestimated. Noninvasive methods, like manual compression and UGCT, should remain the first-line treatment as they offer a high success rate, are easily available, and have low complication rates.\(^9\) There are several invasive alternatives available for cases where these techniques fail or are not feasible, each with its own advantages and drawbacks.

Surgical treatment should be avoided whenever possible as it is associated with a high complication and mortality rate.\(^10\) A prospective study of San Norberto García et al. found that 71% of patients experienced some type of postoperative complication after surgical treatment of a PSA, including the need for transfusion,
The most common invasive technique for PSA treatment is UGTI, with high success rates ranging from 92% to 100%. One major limitation of this method is the anatomy of the PSA, regarding neck width and length as well as sack size, as there is a risk of embolism due to the retrograde flow within the neck of the PSA. The presented technique of BATI was used for patients where these limitations made conventional UGTI unfeasible. With the additional support of balloon occlusion, a high success rate of 93% for PSA treatment was achieved in these complex cases. For the two remaining patients, where only partial thrombosis was achieved, additional UGTI was sufficient due to the size reduction after BATI. One small embolism was encountered after PSA treatment with BATI, located in a side branch of the deep femoral artery. The patient was asymptomatic, and no further treatment was required. As this complication was only detectable on the angiogram after treatment, it could be possible that small arterial embolisms after UGTI are more common than reported.

Recurrences after PSA treatment with BATI occurred in four patients. Surgery was only performed in one of these patients, due to an additional arterio-venous fistula that required treatment. The other three cases could be treated with interventional methods alone. Comparison of recurrence rates to other methods is difficult because they are rarely reported and follow-up is often missing.

There have been reports of other new methods for interventional PSA repair, which involve the interventional insertion of a VCD after primary closure, but the experience with these techniques is currently limited. This study presents the extensive experience with BATI gathered over the last 3 years at our institution, including patients after a wide variety of initial procedures. High success and low complication rates were achieved for this heterogeneous group, even under anticoagulant or antiplatelet treatment.

Radial and brachial PSAs are rare complications and experience regarding treatment is limited. Although most of the afflicted vessels in this study were femoral arteries, two radial, and two brachial arteries were also successfully treated without complications.

### 4.2 Treatment of active bleeding

Although a comparable method for PSA repair has been described in 1998 for a small group of patients by Loose and Haslam, there is no previously reported implementation of BATI for cases with active noncompressible bleeding. The presented technique showed very promising results for this application with a primary success rate of 96%. Achievement of complete hemostasis failed in only one case, where the TISSEEL was injected adjacent to the bleeding channel. This led to a sufficient stop of the bleeding and the remaining cavity was occluded with conventional UGTI the following day. No recurrence of active bleeding occurred, but in two cases a PSA formed after the index procedure. Successful closure was achieved for one of these with manual compression and the other with UGTI.

Regarding complications, one peripheral embolism was observed in this group that had to be treated with a stent-graft. As this complication showed in the final imaging after initially salvaging a dislocated MANTA® device during the same procedure, the exact cause of the embolism remains uncertain.

The list of alternative treatment options for noncompressible access site bleeding is limited. Surgery should always remain the last resort, due to the high complication and mortality rates.

The most common interventional alternative is the implantation of a covered stent in the afflicted artery. Although short-term experiences with this method are promising, the potential downsides of stent implantation, like stent fracture and stenosis need to be considered. Current recommendations for interventional treatment of peripheral artery disease discourage the usage of stent-grafts in bending areas like hip and knee joints. The stress on the material in the groin might be decreased in the typically elderly population of TAVR patients, but with the indication for TAVR being extended to younger and more active patients, this aspect could become more relevant. Balloon-assisted fibrin sealant injection on the other hand offers the advantage of primarily circumventing the introduction of
foreign material in an otherwise healthy vessel while retaining the option of stent implantation for bail-out.

4.3 | Procedural aspects

A crucial aspect is to ensure complete balloon occlusion of the afflicted artery before fibrin sealant injection, to minimize the risk of peripheral embolism or thrombosis. Angiography is sufficient for most cases, but we recommend an additional injection of contrast through the correctly positioned needle during balloon inflation, if there are any uncertainties.

The most difficult part of the procedure is the positioning of the needle before TISSEEL injection. Particularly in the case of active bleeding, the puncture of the bleeding channel can be quite challenging, but this study showed that an experienced operator can perform this task safely and reliably. Fluoroscopic guidance is essential for the correct placement of the needle, but the proximity leads to higher radiation exposure of the operator. The dose-area product for the procedures varied widely and depended mainly on the target vessel, as was to be expected, but it was overall comparable to other peripheral interventional procedures.

Other drawbacks of the method are the necessity of new vascular access and contrast agent exposure. No complications were encountered regarding the additional puncture sites and the median contrast agent use of 41 ml is acceptable. A median procedure duration time of 27 min is reasonable for the treatment of access site complications and makes routine use of this method feasible.

The treatment was conducted through a radial approach in 27% of the cases. The rationale of the radial and especially distal radial access is to avoid further adverse events in patients with already existing vascular complications and to simplify the access in the iliac artery in case of difficult anatomy of the aortic bifurcation. The disadvantage of transradial access is the limited availability of peripheral balloon catheters with very long working lengths (150 cm and longer) and large diameters (up to 10–12 mm). Furthermore, there are no covered stents with such length and suitable diameter available for bail-out.

Different thrombogenic substances have been used for interventional PSA treatment. TISSEEL fibrin sealant (Baxter International) was used in this study for UGTI and BATI as the two active components (Sealer Protein and Thrombin) lead to a fast clot formation that is mainly independent of the coagulation factors of the patient. The patients’ consent has to be obtained for this off-label usage.

4.4 | Limitations

There are some shortcomings of this analysis. Growing experience during the reported period could have influenced the decision-making and chosen technique of treatment.

The next important limitation is the single center character of the analysis. Only well-experienced operators very familiar with different techniques of thrombin injection were involved in the decision-making and in the procedures.

Unfortunately, it is difficult to simplify and standardize the contraindications for simple UGTI and the indications for BATI, due to the multifactorial character of the decisions with the high impact of individual experience of the operators. Due to the small number of events and limited cohort size, the power to detect significant associations of risk factors with failure, recurrence, or complications is low. Therefore, the fact that we did not find any significant association does not exclude such.

5 | CONCLUSIONS

The reported technique of BATI seems to be feasible and safe if performed by experienced operators and enables management even of substantial wall defects after large-bore access with good results.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Jakob U. Lindner http://orcid.org/0000-0002-2015-968X

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