Review Article

Access site complications in transcutaneous aortic valve replacement: frequency, outcomes, prevention, and treatment

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Abstract: Aortic stenosis (AS) is a common cause of valvular heart disease with heavy disease burden in elderly patients. It is present in almost 7% of patients older than 65. The mortality rate increases significantly once it becomes symptomatic with average life expectancy of around 1-year. Symptoms include angina, syncope, or heart failure. This requires either surgical or transcutaneous replacement. Transcutaneous aortic valve replacement (TAVR) use has increased in recent years from high risk patients to now even including intermediate risk patients. With the increased number of procedures performed, one of the consequences is access site complications. These complications can lead to increased hospitalization, cost, infections, and eventually worse outcomes. In this manuscript, we provide a comprehensive review discussing the consequences, outcomes, frequency, predictors and some possible solutions to these complications set forth in these studies.

Keywords: Transcutaneous aortic valve replacement (TAVR); access site; complications

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Introduction

There are several recent studies addressing access site complications that occur during transcutaneous aortic valve replacement (TAVR) procedures, which can lead to increased hospitalization, cost, infections, resulting in worse outcomes. Herein, we provide a comprehensive review discussing the consequences, outcomes, frequency, predictors and some possible solutions to these complications described in these studies.

Aortic stenosis (AS)

AS is a prevalent cause of valvular heart disease in elderly patients. It is present in around 7% of patients older than 65 (1,2). Once symptomatic, the mortality rate increases significantly with average life expectancy of around 1-year. Symptoms include angina, syncope, or heart failure (3,4).

In the United States, the most common cause of AS is degeneration and valvular calcification (>50%), Other important causes include bicuspid valve disease representing 30–40% of cases; which is seen in younger populations (5-7) and rheumatic heart disease more commonly seen in developing countries.

For years, the standard therapy for AS has been surgical replacement of the aortic valve. This improved survival and reduced morbidity; however only patients with acceptable surgical risk were considered to be good candidates (8,9).

In recent years, as the patient population is aging with the encounter of more high-risk candidates, several trials have shown TAVR (10,11) to be effective and comparable as surgical treatment for severe symptomatic AS, mostly in

patients that are considered high risk; such as patients with multiple co-morbidities and previous sternotomies.

The PARTNER 2 trial compared surgical aortic valve repair (SAVR) versus TAVR. Two-year follow up in patients treated with TAVR have been comparable to those treated with SAVR. This data has lead the FDA to approving TAVR use in intermediate risk patients (12). This new approval will possibly lead to facing increased complications since more patients will undergo TAVR. Based on this data, new research is coming out concerning for the use of TAVR in low risk patients (13). As these studies come to fruition, with results that show early comparable results between SAVR and TAVR, more procedures will be performed with the side effect of more complications.

As the need for TAVR increases, it is pertinent to address complications associated with this procedure. One such important complication is what is seen at the vascular access site. These are usually benign but can be serious enough to lead to serious adverse outcomes, and hence increasing mortality and morbidity.

Defining access site and bleeding complications

In 2010, the Valve Academic Research Consortium (VARC) first published a consensus concerning clinical endpoints for research involving TAVR. These definitions consist of many different endpoints including vascular access site and bleeding complications. Both endpoints are important to the studies included.

Vascular complications were split into major and minor. Differences include amount of blood transfusion (≥4 units), need for intervention, and end organ damage.

Bleeding was categorized into three groups, life-threatening, major, and minor. Life-threatening was defined fatal bleeding, or bleeding in a critical area or organ, bleeding causing hypovolemic shock or severe hypotension requiring vasopressors, surgery or overt source of bleeding with drop in hemoglobin ≥5 g/dL or transfusions ≥4 units. Major bleeding was defined as overt bleeding associated with drop in hemoglobin of at least 3 g/dL or requiring transfusion of 2 or 3 units AND does not meet criteria of life-threatening bleeding. Minor bleeding is defined as bleeding worthy of mention but does not include the other two categories (14).

In 2012, VARC-2 was released. As far as bleeding, the criteria did not change. Information was updated concerning vascular access site complications. Preplanned closure device use was not considered as a complication. The committee recommended that the use of accurate documentation concerning plans should be made (15).

Access site complications-epidemiology

Reviewing the major trials, it is easy to assess the number of patients affected by access site complications defined previously by the VARC definitions. In WIN TAVI, VARC Major accounted for 7.7% of bleeding complications and VARC life-threatening accounted for 4.4% (16). This was a particularly interesting study because it looked at acute and 30-day outcomes in women undergoing TAVR; which is important as shown later in this manuscript. In PARTNER, 17% of the patients undergoing TAVR had a vascular complication and 9.3% had a major bleed (11). In PARTNER 2, 7.9% of the patients receiving at TAVR had a major vascular complication and 10.4 had life-threatening or disabling bleeding. As it was demonstrated, vascular complications and life-threatening bleeding account for significant problems encountered during TAVR procedures.

Risk factors for complications

Multiple studies over the past several years have demonstrated the importance of risk factors for access site complications. Female gender and sheath size >19 French have been shown in several studies to increase risk. First, Van Mieghem *et al.* showed that female gender was an independent predictor for complications (17). This study was a five-center study with 803 patients undergoing transfemoral approach. Soon, thereafter, Généreux *et al.* again showed female gender as a risk factor for major bleeds (18). In another study, 62% of patient that had access site bleeding in their patient population were females (19). Another risk factor shown in these studies is the size of the sheath being >19 French. In 22% undergoing TAVR with a >19 French sheath had major vascular complications and 16% had life-threatening bleed. 20% required bailout intervention. Hine *et al.* showed age as a risk factor for complications with the difference in complication increasing by 7% with a year's difference (19).

Frequency and consequences of access site complications

One of the complications that can occur during TAVR procedure is pseudoaneurysm and bleeding. This can lead to infections, recurrent hospitalizations, transfusions, and

possibly death. Recently, Piccolo *et al.* (20) in a single center study looked at comparing access site vs non-access site bleeding frequency and outcomes. Obvious data noted from this study was the high frequency of access site bleeds, reaching up to 15%. This was further differentiated into life-threatening (47%), major (59%), and minor bleeding (38%). Not surprisingly, life-threatening and major bleeds led to increased mortality compared to no bleeding. Because of the 5-year follow up in this study, timing of bleeds was also quantified. All access site bleeds occurred within the first 30 days following the procedure. The researchers were also able to track 5-year mortality between the three groups, proving that access-site bleeds lead to an increased mortality even in the long term. Packed red blood cell (PRBC) transfusions were used in 44% of those patients with access site complications. Transfusions were associated with increased mortality when compared to no need for transfusions (19). In one study, Core valve accounted for 56% of access-site bleeding, Sapien XT 39%, Sapien 32.1%, Acurate 1.4%, and finally both Portico and Lotus each 0.7% (19). In the PARTNER trial, where the Edwards Sapien Valve was used, vascular complications were shown in 15% of the patients.

These studies show that while TAVR typically helps treat AS in patients with prohibitive risk, sometimes the complications associated with the procedure may lead to similar outcomes as seen with SAVR.

It is also important to highlight several predictors of outcomes. As discussed before, life-threatening and major bleeds certainly increased mortality. Furthermore, as previously demonstrated, the use of PRBC transfusions can lead to increased mortality.

Access site injuries of TAVR

Access site hematomas are one of the more common complication. These can occur anytime post-procedure. Most of the time, these can be managed conservatively and resolve spontaneously. Hematomas will be reported because of persistent pain. Ultrasonography can be used to evaluate and to rule out pseudoaneurysm (21). In PARTNER, access site hematoma accounted for 22.9% of the major complications (18).

Pseudoaneurysms are pulsatile hematomas that communicate with an artery. This occurs because of injury to the arterial wall. Post-procedure angiography of the iliac-femoral arteries can reveal arterial leak. This is a precursor. Pseudoaneurysms typically present with pain. Diagnosis is suspected with new bruit or thrill near the access site and is confirmed by ultrasound. Again, PARTNER showed that pseudoaneurysm accounted for 3.4% of the major complications (18).

In patients undergoing transfemoral approach, dissection is one of the most common complications. It was reported in about 6.5% of patients (18). This typically occurs during placement of sheath. Dissection may cause vascular compromise of the lower extremities. The worst complication that can occur using the transfemoral approach is femoral artery rupture. Rupture is a life-threatening complication and requires timely intervention.

Prevention of access site complications

Access site complications have long term consequences. Several studies have been done to address potential prevention of such adverse events. Prevention can be achieved by increased operator experience, the use of arteriotomy closure devices (ACD), a surgical cut down (SCD), and crossover balloon occlusion technique (CBOT). As expected, with greater experience and an increased number of procedures will culminate into decreased complications. One study compared procedure volume to adverse events. More volume was associated with less adverse outcomes including vascular complications and bleeding (22). This is an interesting look at prevention and argues for more specialized sites with high volume, allowing cardiologists to further perfect their techniques.

Another prevention model is type of access and closure involved during the TAVR. ACDs are devices used with a transcutaneous route. This involves closure of an arterial puncture that measures 12 French or greater. In several studies, this was defined as an incision of 1–2 cm and remote closure of the puncture.

SCD was defined as an incision that lead to visual access and puncture of the common femoral artery (CFA). This was followed at the end of the case with arterial suture or fascial closure technique.

Vierhout *et al.* looked at ACDs versus SCD. The use of ACDs allowed minimally invasive access to the CFA. This study unfortunately did not show clear benefit of either technique. ACDs showed advantage in prevention of post-operative surgical site infections, while SCD indicated benefit in prevention of pseudoaneurysm formation. However, overall ACDs showed slight advantage with a lower percent of complications (6.8%) versus SCD (8.0%) (23). Unfortunately, this study had some limitations,

including sample size and complication reporting.

Another prevention technique studied was the CBOT; which consists of passing a long crossover balloon catheter from the contralateral femoral artery to assist in closure of access sites. This technique enabled the balloon to be inflated before the removal of the delivery sheaths and closure of the arteriotomy sutures. Zaman *et al.* compared CBOT versus no CBOT. This studied used the VARC-2 criteria mentioned earlier as primary endpoints. The study showed a reduction in access related complication; which occurred in 5.5% of the CBOT group and 18.6% in the control group (24).

We re-emphasize the importance of prevention in further reducing the number of access site complications. This includes more operator experience, the appropriate use of closure devices and sometimes CBOT.

Treatment of access site complications

Treatment of access site complications can be divided into percutaneous intervention such as stent grafts versus vascular surgery.

As discussed earlier, access site bleeding is very detrimental. If pre-closure of the arterial puncture site fails or artery site perforation occurs, immediate intervention is required to avoid potentially life-threatening bleeding. When this occurs, the first step is temporary hemostasis. Following that, access can be established from the contralateral ilio-femoral artery. Angiography under fluoroscopic guidance is then used to localize the lesion or perforation and subsequent insertion, advancement via fluoroscopy and deployment of the stent graft. Other treatments include balloon angioplasty and the need for direct intervention with surgery.

In smaller injuries to the femoral artery, the use of balloon angioplasty is warranted. The use of a catheter in the contralateral side to pass a balloon to achieve hemostasis as this can help prevent the formation of large hematomas. For larger injuries, stent grafts are preferred as discussed below.

In those patients that are unable to achieve hemostasis via manual compression or balloon angioplasty without the option for stent graft or operator determination, the ability for surgical repair is available. Surgical repair includes suturing the defect or using a patch for angioplasty with direct visualization.

Several studies have reported good outcomes using the Viabahn stent graft, which is a self-expanding endoprosthesis. Segal et al, in a single center study looked at the use of stent graft implantation for vascular repair in access site complications. It was found that such grafts prevented the need for vascular surgery as well as preventing further vascular compromise. When compared to vascular surgery, stent graft implantation was not associated with higher mortality or renal failure. Stent grafts were used in 91% of the complications (25). Another study, by De Backer *et al.*, looked at the use of Viabahn endoprosthesis for vascular access complications. This was a single center observation study. It showed good outcomes in both short-term and medium-term outcomes. Out of 348 patients, 72 had vascular access complications. Treatment was further divided into balloon angioplasty (25%), Viabahn stenting (67%), or surgical intervention (8%) based on the operator discretion. Vascular access complication was defined using VARC-2 discussed earlier. Length of stay and thirty-day mortality was similar in the control and Viabahn subgroups. As this was an observational study, it does not give definitive answers concerning access site complications, however it demonstrates an effective and safe treatment for such complications (26).

Steinvil *et al.* further clarified the use of the Viabahn endoprosthesis as a treatment for access site complications. That study looked at its use in pre-closure device failure. In the 25 patients observed the Viabahn stent performed optimally. Patients did not have a significant rate of adverse events or mortality. This study further validated the use of endoprosthesis in the treatment of vascular access site complications (27). As TAVR procedures become more widely used, treatment for complications will need to be compared and studied. These studies help show safe and effective ways to treat these complications

Conclusions

Access site complications are the Achilles heel of TAVR procedures, potentially leading to severe bleeding, prolonged hospitalization, increased morbidity and mortality. potential risk factors including female gender, size of the catheter, increased operator experience and advanced age increase the risk of developing this complication.

Different closure devices have been key to help in prevention of such complications. A diverse range of treatment modalities including balloon angioplasty, endoprosthesis stent graft and surgery have also been used in such complications.

More studies are needed to confirm these risk factors and

treatments for access site complications in TAVR patients.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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