Computed tomography defined femoral artery plaque composition predicts vascular complications during transcatheter aortic valve implantation

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Abstract

Purpose

Vascular and bleeding complications after transcatheter aortic valve implantation (TAVI) are common and lead to increased morbidity and mortality. Analysis of plaque at the arterial access site may improve prediction of complications.

Methods

We investigated the association between demographic and procedural risk factors for Valve Academic Research Consortium (VARC) vascular complications, as well as a novel method of quantifying plaque composition of the common femoral artery using computed tomography angiography plaque maps created with patient specific x-ray attenuation cut-offs. The relationship between time to haemostasis after TAVI with demographic and procedural risk factors was also investigated.

Results

Twenty-three vascular complications occurred in the 299 patients in the study group (7.7%). There were no demographic risk factors associated with vascular complications and no statistical difference between use of closure device (ProGlide® vs MANTA®) and vascular complications. Vascular complications after TAVI were significantly associated with sheath size (OR 1.36, 95% CI 1.08–1.76, P 0.01) and strongly associated with necrotic core volume in the common femoral artery of the procedural side (OR 17.49, 95% CI 1.21–226.60, P 0.03). The use of the ProGlide® closure device (T 2.99, P 0.004) rather than MANTA® was significantly associated with an increased time to haemostasis after TAVI.

Conclusion

Plaque map analysis of plaque composition of the common femoral artery by CT angiography reveals patients with greater necrotic core are at increased risk of VARC vascular complications.

Introduction

Transcatheter aortic valve implantation (TAVI) is an alternative to surgical aortic valve replacement, frequently used in high-, and intermediate-risk patients[1]–[5]. Advances in the procedure and technology including vascular closure devices (VCDs), such as the suture based ProGlide® and plug based MANTA® devices allow it to be performed entirely percutaneously. However, complications associated with vascular access[6]–[11] and bleeding[12]–[18] still occur and result in significant increases in morbidity and mortality. Therefore, the Valve Academic Research Consortium (VARC) have defined clinical endpoints for vascular access site & access-related complications, bleeding & transfusion[19], [20].
Previous studies have investigated demographic and procedural risk factors associated with VARC Vascular Access Site & Access-Related Complications, demonstrating that female sex[21] and sheath to femoral artery ratio (SFAR)[6] and anatomical features such as distance from common femoral artery (CFA) to skin[22] and tortuosity[23] are significantly associated with an increased risk of VARC vascular complications. Arterial calcification defined by computed tomography (CT) imaging is also a risk factor for vascular complications[6, 22, 24]. However, to date only qualitative measures of calcification have been utilised. The role of other non-calcified plaque components as a risk factor for VARC vascular access site & access-related complications is not known.

We have previously described CT angiography lumen contrast / plaque attenuation ratios that can discriminate calcified plaque, fibrous plaque and necrotic core[25]. In this study, we investigate whether identifying quantitative plaque composition from CT-derived plaque maps of the common femoral arteries created using these ratios predicted risk of VARC Vascular access site & access-related complications in patients undergoing transfemoral TAVI access with VCD closure.

Materials & Methods

Patient Selection and Procedure

In this single centre, retrospective cohort study all sequential patients who had undergone transcatheter aortic valve implantation (TAVI), between 21st March 2017 and 12th August 2020 (n = 333) at our institute were considered for inclusion. For inclusion into the study, patients were required to have undergone both a computed tomography (CT) planning scan (including the ilio-femoral arteries), and then felt to be suitable percutaneous transfemoral access and closure with a vascular closure device (VCD).

Sixteen patients were excluded as their ilio-femoral arteries were imaged by catheter angiography, not CT. Patients were considered ineligible for transfemoral access if the ilio-femoral diameter was ≥ 5mm due to atherosclerotic plaque or small calibre arteries and these underwent alternative access TAVI (n = 9) and were excluded. Patients were excluded from VCD if there was anterior wall calcification in the common femoral at the anticipated puncture site of the common femoral artery (n = 7). Finally, patients were excluded from the study if they had previous peripheral vascular surgery (n = 1) or stenting (n = 1). Therefore, 299 patients were included after the above exclusion (see Fig. 1). The VCD device (ProGlide® or MANTA®) was chosen at the operators’ discretion.

The side of large-bore device insertion was determined by the operator after reviewing the CT images to obtain a combination of maxim lumen diameter and minimal arterial disease and tortuosity. All punctures were performed with ultrasound guidance and the location in the common femoral artery confirmed fluoroscopically. Patients undergoing closure using a MANTA® VCD received a single 18 French device. Patients undergoing closure using ProGlide® received x2 pre deployed devices as default but could receive additional ProGlide® devices as required to achieve haemostasis. Baseline characteristics were
obtained from a dedicated TAVI database, which was completed with patients’ information at the time of the procedure.

**Preliminary CT Analysis**

Patients had a TAVI planning CT angiogram, which consisted of an electrocardiogram (ECG)-gated Cardiac CT and a contrast enhanced helical scan of the whole aorta to below the femoral artery bifurcation to establish procedural feasibility. Images were analysed using Vitrea® Software Version 7.14.5.13 (Vital Images, Inc.).

The antero-posterior diameter of the common femoral artery (CFA) was measured manually at the mid-femoral head, whilst distance to skin from the CFA was measured from the most anterior point of the CFA perpendicular to the skin surface at the mid-femoral head. The length of the arterial vessels was measured from the most proximal point of the common iliac artery to the most distal point of the common femoral artery. Tortuosity was expressed as the tortuosity index, which is the true length of these vessels divided by the straight-line distance.

**Plaque Composition CT Analysis**

The common femoral artery was analysed on the side of TAVI valve insertion. The upper and lower limits were defined with the upper limit the origin of the inferior epigastric artery and the lower limit the most distal point of the common femoral artery prior to the femoral bifurcation. Attenuation (Hounsfield Units) of contrast of the lumen was sampled at the mid-femoral head. The attenuation cut-offs for each plaque component were calculated according to ratios of luminal contrast and plaque attenuation (necrotic core < 0.197, fibrous plaque 0.197–0.470, calcified plaque > 1.295) derived using histological validation and described in details previously[25]. This sets attenuation thresholds for plaque components individualised to each patient. These are used by the Vitrea® software to create plaque maps of the common femoral arteries allowing the volumes of the necrotic core, fibrous plaque and calcified plaque to be calculated (Fig. 2).

The artefact created by a hip replacement on the same side as the TAVI procedure interferes with attenuation base plaque analysis so these patients (29) were excluded from analysis of plaque composition in the study. Some patients (3), despite having sufficient contrast to carry out preliminary CT analysis, did not have sufficient contrast for advanced plaque analyse of the common femoral artery. Therefore, 267 patients were included in the analysis of plaque composition.

**Endpoints**

**Vascular Access Site & Access-Related Complications**

The primary end point of the study was a composite of major vascular complications and minor vascular complications as determined by the Valve Academic Research Consortium (VARC) vascular access site & access-related complications definitions as shown in Fig. 3[19], [20].
Major vascular complications

- Any aortic dissection, aortic rupture, annulus rupture, left ventricle perforation, or new apical aneurysm/pseudo-aneurysm OR
- Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysms, haematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) leading to death, life-threatening or major bleeding*, visceral ischaemia, or neurological impairment OR
- Distal embolization (non-cerebral) from a vascular source requiring surgery or resulting in amputation or irreversible end-organ damage OR
- The use of unplanned endovascular or surgical intervention associated with death, major bleeding, visceral ischaemia or neurological impairment OR
- Any new ipsilateral lower extremity ischaemia documented by patient symptoms, physical exam, and/or decreased or absent blood flow on lower extremity angiogram OR
- Surgery for access site-related nerve injury OR
- Permanent access site-related nerve injury OR

Minor vascular complications

- Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysms, haematoma, percutaneous closure device failure) not leading to death, life-threatening or major bleeding*, visceral ischaemia, or neurological impairment OR
- Distal embolization treated with embolectomy and/or thrombectomy and not resulting in amputation or irreversible end-organ damage OR
- Any unplanned endovascular stenting or unplanned surgical intervention not meeting the criteria for a major vascular complication OR
- Vascular repair or the need for vascular repair (via surgery, ultrasound-guided compression, transcatheter embolization, or stent-graft) OR

Percutaneous closure device failure

- Failure of a closure device to achieve haemostasis at the arteriotomy site leading to alternative treatment (other than manual compression or adjunctive endovascular ballooning)

*Refers to VARC bleeding definitions

Time to Haemostasis

The secondary outcome from the study was the time to haemostasis, which was measured in seconds and defined as the time from beginning of VCD deployment until successful haemostasis obtained at the
access site. Patients in whom VCD was used for closure were also compared to a historical cohort that underwent the gold standard of surgical closure to compare vascular complication rates and time to haemostasis (Supplemental Material).

**Statistical Analysis**

Statistical analysis was performed using Prism 9, GraphPad (GraphPad Software, San Diego, United States). Unpaired Student’s “t” test was used to compare continuous variables and the Fisher’s exact test was used to compare proportions of categorical variables. Pearson correlation coefficient was used to compare two continuous variables. Multivariate analysis was carried out using multiple logistic regression for categorical data and multiple linear regression for continuous data. Differences in data were expressed as an odds ratio (OR) with 95% confidence limits (CI). A 2-sided P < .05 was deemed significant for all statistical tests.

**Results**

**Baseline Characteristics**

Baseline characteristics for the 299 patients undergoing TAVI procedure with vascular closure devices between 1st October 2016 and 12th August 2020 are presented in Table 1.
Of the patients undergoing a TAVI procedure, 235 (78.6%) were closure with the MANTA® device, whilst 64 (21.4%) of patients had closure with ProGlide® devices. The majority of patients receiving ProGlide® devices 53/64 (83%) achieved haemostasis with two devices. Additional ProGlide® devices were required in nine patients (14%), with seven patients requiring three ProGlide® devices and 2 patients requiring five ProGlide® devices to achieve haemostasis.

One hundred and forty-five (48.5%) patients were male and the average age was 83.1 ± 6.9 years (mean ± standard deviation). Overall, there were 7 in-hospital deaths (2.3%) following the procedural group, of which 1 (0.003%) was related to an access site complication.

There were 11 VARC major events (3.7%) and 12 VARC minor events (4%) meaning the primary endpoint was met in 23 patients (7.7%) (see Table 2).
Table 2
Description of VARC major and minor events, demonstrating vascular closure device used, valve type implanted, valve size implanted and sheath size used in each instance

| VARC Major Events |
|-------------------|-----------------|-----------------|-----------------|-------------------|
| Closure Device    | Valve Type      | Valve Size (mm) | Sheath Size (Fr)| VARC Major Event              |
| ProGlide®         | Portico         | 29              | 19              | Retroperitoneal haematoma with major (BARC 3a) bleeding |
|                   |                 |                 |                 | Percutaneous closure device failure with major (BARC 3a) bleeding |
| ProGlide®         | Portico         | 27              | 19              | i. Iliac artery bleeding with life-threatening (BARC 3b) bleeding |
|                   |                 |                 |                 | ii. Percutaneous closure device failure |
| ProGlide®         | Portico         | 29              | 19              | Pseudoaneurysm requiring surgical repair and major (BARC 3a) bleeding |
| MANTA®            | Sapien 3        | 26              | 14              | Percutaneous closure device failure with life threatening (BARC 3b) bleeding |
| MANTA®            | Portico         | 27              | 19              | i. Percutaneous closure device failure with major (BARC 3a) bleeding |
|                   |                 |                 |                 | ii. Dissection with major (BARC 3a) bleeding |
| MANTA®            | Sapien 3        | 23              | 14              | Retroperitoneal haematoma with fatal (BARC 5) bleeding |
| MANTA®            | Sapien 3        | 26              | 19              | Pseudoaneurysm with major (BARC 3a) bleeding |
| MANTA®            | Portico         | 27              | 19              | Retroperitoneal haematoma with major (BARC 3a) bleeding |
| MANTA®            | Portico         | 29              | 19              | Percutaneous closure device failure with fatal (BARC 5) bleeding |
| MANTA®            | Sapien 3        | 26              | 14              | Pseudoaneurysm requiring surgical repair |

| VARC Minor Events |
|-------------------|-----------------|-----------------|-----------------|-------------------|
| Closure Device    | Valve Type      | Valve Size (mm) | Sheath Size (Fr)| VARC Minor Event |
| ProGlide®         | Portico         | 29              | 19              | Femoral dissection managed conservatively |
| ProGlide®         | Portico         | 25              | 18              | Femoral occlusion requiring endovascular ballooning |
### VARC Major Events

<table>
<thead>
<tr>
<th>Closure Device</th>
<th>Valve Type</th>
<th>Valve Size (mm)</th>
<th>Sheath Size (Fr)</th>
<th>VARC Major Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>ProGlide®</td>
<td>Sapien 3</td>
<td>29</td>
<td>16</td>
<td>Femoral dissection requiring endovascular ballooning</td>
</tr>
<tr>
<td>ProGlide®</td>
<td>Sapien 3</td>
<td>23</td>
<td>18</td>
<td>Retroperitoneal haematoma with minor (BARC 2) bleeding</td>
</tr>
<tr>
<td>MANTA®</td>
<td>Sapien 3</td>
<td>23</td>
<td>14</td>
<td>Arterial clot managed conservatively, later re-admitted with ischaemic limb requiring vascular surgery</td>
</tr>
<tr>
<td>MANTA®</td>
<td>Portico</td>
<td>29</td>
<td>19</td>
<td>Pseudoaneurysm managed conservatively</td>
</tr>
<tr>
<td>MANTA®</td>
<td>Portico</td>
<td>25</td>
<td>18</td>
<td>Arterial clot managed conservatively</td>
</tr>
<tr>
<td>MANTA®</td>
<td>Sapien 3</td>
<td>29</td>
<td>16</td>
<td>Femoral dissection requiring endovascular ballooning</td>
</tr>
<tr>
<td>MANTA®</td>
<td>Sapien 3</td>
<td>23</td>
<td>14</td>
<td>Femoral dissection requiring endovascular ballooning</td>
</tr>
<tr>
<td>MANTA®</td>
<td>Allegra</td>
<td>27</td>
<td>18</td>
<td>Femoral dissection requiring endovascular ballooning</td>
</tr>
<tr>
<td>MANTA®</td>
<td>Portico</td>
<td>27</td>
<td>15</td>
<td>Femoral dissection requiring endovascular ballooning</td>
</tr>
<tr>
<td>MANTA®</td>
<td>Portico</td>
<td>25</td>
<td>14</td>
<td>Femoral dissection &amp; occlusion requiring endovascular ballooning</td>
</tr>
</tbody>
</table>

VARC = Valve Academic Research Consortrium

BARC = Bleeding Academic Research Consortium

The VARC major events that occurred were percutaneous closure device failure with fatal bleeding (1), percutaneous closure device failure with life-threatening bleeding (2), percutaneous closure device failure with major bleeding (2), retroperitoneal haematoma with fatal bleeding (1), retroperitoneal haematoma with major bleeding (2), pseudoaneurysm with major bleeding (1), pseudoaneurysm requiring surgical repair and major bleeding (1), and pseudoaneurysm requiring surgical repair (1).

The VARC minor events that occurred were femoral dissection requiring endovascular ballooning (5), femoral occlusion requiring endovascular ballooning (1), femoral dissection & occlusion requiring endovascular ballooning (1), femoral dissection managed conservatively (1), retroperitoneal haematoma with minor bleeding (1), arterial clot managed conservatively (2), and small pseudoaneurysm of femoral artery managed conservatively (1).

### Demographic & Procedural Risk Factors for Composite Outcome
Comparison of demographic risk factors did not demonstrate any significant associations with increased number of VARC outcomes (see Table 3a). Regarding procedural risk factors, we found that there was no significant association with the use of ProGlide® over MANTA®, the urgency of TAVI procedure, the side of transfemoral access, or hip replacement having been previously performed on the same side as TAVI access (see Table 3b). We found a significant difference with an increased sheath size used in the procedure and the composite of VARC outcomes (T 2.29, p 0.02).

Table 3
a: Demographic Risk Factors for Composite Outcome

<table>
<thead>
<tr>
<th></th>
<th>No VARC</th>
<th>%</th>
<th>End-Point Met</th>
<th>%</th>
<th>Univ.</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL</td>
<td>276</td>
<td>-</td>
<td>23</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>136</td>
<td>49.3%</td>
<td>9</td>
<td>39.1%</td>
<td>OR</td>
<td>0.66</td>
</tr>
<tr>
<td>Age (years)</td>
<td>83.1 +/- 7.0</td>
<td>-</td>
<td>84.3 +/- 5.4</td>
<td>-</td>
<td>T 0.85</td>
<td>P 0.40</td>
</tr>
<tr>
<td>Diabetes</td>
<td>70</td>
<td>25.4%</td>
<td>5</td>
<td>21.7%</td>
<td>OR</td>
<td>0.82</td>
</tr>
<tr>
<td>Current/Previous Smoker</td>
<td>143</td>
<td>51.4%</td>
<td>13</td>
<td>56.5%</td>
<td>OR</td>
<td>1.21</td>
</tr>
<tr>
<td>Baseline Creatinine (µmol/L)</td>
<td>108.1 +/- 60.4</td>
<td>-</td>
<td>105.3 +/- 25.0</td>
<td>-</td>
<td>T 0.22</td>
<td>P 0.83</td>
</tr>
<tr>
<td>Previous MI</td>
<td>46</td>
<td>16.7%</td>
<td>7</td>
<td>30.4%</td>
<td>OR</td>
<td>2.19</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.7 +/- 5.6</td>
<td>-</td>
<td>27.8 +/- 5.6</td>
<td>-</td>
<td>T 0.90</td>
<td>P 0.37</td>
</tr>
</tbody>
</table>

Mean +/- SD
Table 3
b: Procedural Risk Factors for Composite Outcome

<table>
<thead>
<tr>
<th></th>
<th>No VARC</th>
<th>%</th>
<th>End-Point Met</th>
<th>%</th>
<th>Univ.</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TOTAL</strong></td>
<td>276</td>
<td>-</td>
<td>23</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ProGlide®</td>
<td>56</td>
<td>20.3%</td>
<td>8</td>
<td>34.8%</td>
<td>OR 2.10</td>
<td>P 0.11</td>
</tr>
<tr>
<td>Urgent Procedure</td>
<td>87</td>
<td>31.5%</td>
<td>8</td>
<td>34.8%</td>
<td>OR 1.16</td>
<td>P 0.82</td>
</tr>
<tr>
<td>Right Transfemoral Access</td>
<td>207</td>
<td>75.0</td>
<td>18</td>
<td>78.3%</td>
<td>OR 1.20</td>
<td>P &gt; 0.99</td>
</tr>
<tr>
<td>Procedural Side Hip Replacement</td>
<td>25</td>
<td>9.1%</td>
<td>4</td>
<td>17.4%</td>
<td>OR 2.11</td>
<td>P 0.26</td>
</tr>
<tr>
<td>Sheath Size (Fr)</td>
<td>16.1 +/- 2.0</td>
<td>-</td>
<td>17.1 +/- 2.2</td>
<td>-</td>
<td>T 2.29</td>
<td>P 0.02*</td>
</tr>
</tbody>
</table>

VARC: Vascular Access-Related Complication, SD: standard deviation, MI: myocardial infarction, BMI: body mass index

Preliminary CT Analysis for Composite Outcome

Similarly, regarding our preliminary analysis of CT images, there was no significant association found between the composite of VARC outcomes and diameter of the common femoral artery, perpendicular distance from CFA to skin, or tortuosity of the vessel (see Table 4).

Table 4
Preliminary CT Analysis Risk Factors for Composite Outcome

<table>
<thead>
<tr>
<th></th>
<th>No VARC</th>
<th>End Point Met</th>
<th>Univ.</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TOTAL</strong></td>
<td>276</td>
<td>23</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CFA Diameter (mm)</td>
<td>8.4 +/- 1.6</td>
<td>7.9 +/- 1.4</td>
<td>T 1.44</td>
<td>P 0.15</td>
</tr>
<tr>
<td>Mean +/- SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distance to Skin (mm)</td>
<td>40.9 +/- 21.4</td>
<td>46.3 +/- 20.4</td>
<td>T 1.16</td>
<td>P 0.25</td>
</tr>
<tr>
<td>Mean +/- SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tortuosity</td>
<td>1.2 +/- 0.1</td>
<td>1.2 +/- 0.1</td>
<td>T 0.25</td>
<td>P 0.80</td>
</tr>
<tr>
<td>Mean +/- SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CFA: common femoral artery, SD: standard deviation

Plaque Composition & Composite Outcome
By identifying the composition of plaque in the vessel, we found a significant association between the volume of necrotic core identified and the composite of VARC outcomes in the common femoral artery ($T = 2.02, p = 0.04$). We did not find any significant association between volume of vessel, plaque burden, total plaque volume, volume of fibrous plaque, or volume of calcification with the composite of VARC outcomes (see Table 5). After multivariate analysis, we found that volume of necrotic core in the common femoral artery (OR 17.49, 95% CI 1.21–226.60, $p = 0.03$) and sheath size (OR 1.36, 95% CI 1.08–1.76, $p = 0.01$) were associated with an increased risk of vascular composite outcome.

<table>
<thead>
<tr>
<th>Table 5</th>
<th>Plaque Composition as Risk Factor for VARC Composite Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No VARC</td>
</tr>
<tr>
<td>TOTAL</td>
<td>248</td>
</tr>
<tr>
<td>Sheath Size (Fr)</td>
<td></td>
</tr>
<tr>
<td>Mean +/- SD</td>
<td>16.05 +/- 2.05</td>
</tr>
<tr>
<td>Sheath Size (Fr)</td>
<td></td>
</tr>
</tbody>
</table>

Common Femoral Analysis

| Volume (cm$^3$) | 4.14 +/- 1.67 | 3.79 +/- 2.21 | $T = 0.86$ | $P = 0.39$ |
| Plaque Burden (%) | 24.47 +/- 10.49 | 23.17 +/- 5.48 | $T = 0.53$ | $P = 0.60$ |
| Total Plaque Volume (cm$^3$) | 1.00 +/- 0.62 | 0.85 +/- 0.34 | $T = 1.09$ | $P = 0.28$ |
| Necrotic Core Volume (cm$^3$) | 0.17 +/- 0.13 | 0.24 +/- 0.25 | $T = 2.02$ | $P = 0.04^*$ |
| Fibrous Plaque Volume (cm$^3$) | 0.42 +/- 0.18 | 0.37 +/- 0.15 | $T = 1.20$ | $P = 0.23$ |
| Calcification Volume (cm$^3$) | 0.42 +/- 0.58 | 0.23 +/- 0.21 | $T = 1.41$ | $P = 0.16$ |

Time to Haemostasis

ProGlide® closure patients had a longer time to haemostasis (21.1 ± 14.8 seconds) compared to MANTA® (16.8 ± 8.8 seconds) closure ($T = 2.91, p = 0.004$). After multivariate analysis of all demographic risk factors, procedural risk factors, as well as preliminary and plaque composition CT analysis, we found a significant association only between the use of ProGlide® closure and increased time to haemostasis ($T = 2.99, p = 0.04$).
Discussion

In this study, we found that there was a vascular complication (as per the VARC criteria[19]) in 7.7% of patients. This was lower than the 21% recorded in two other studies[22], [26]. This may be due in part to the mandated use of ultrasound guided puncture and the exclusion of VCD use in patients with common femoral artery anterior wall calcification. The complication rate was similar (6.6%) to a recent study comparing vascular closure with MANTA® or ProGlide®[27].

In contrast to the above study, which found a significantly lower rate of vascular complications in the ProGlide® group compared to the MANTA® group, we found no significant difference in the percentage of vascular complications using either device (ProGlide® (9.7%) or MANTA® (5.7%), p = 0.11). Our results are supported by other data, which has demonstrated no significant difference between closure devices and vascular complications[28]. We noted that similar types of complications were encountered with the use of each device, with percutaneous closure device failure, retroperitoneal haematoma and pseudoaneurysm occurring in both device types. Similarly, with regards to VARC minor events, femoral dissections and femoral occlusions occurred in both device groups.

There were no significant associations between demographic risk factors and vascular complications in our study. We note that a previous study[12] has identified female sex as a risk factor of vascular complications after TAVI. We did find that increased sheath size was a risk factor for vascular complications at both univariate and multivariate level of analysis. Larger sheath size has previously been reported as a risk factor for vascular complications[12], whilst other studies have also demonstrated a significantly increased risk of vascular complications with an increased sheath to femoral artery ratio (SFAR)[6].

Preliminary analysis of CT imaging, such as CFA diameter, and perpendicular distance from CFA to skin was not a significant risk factor for the composite of VARC major and minor vascular complications. Importantly, we found that an increase in the total necrotic core volume throughout the common femoral artery was an independent risk factor for vascular complications after TAVI.

Although qualitative femoral calcification has previously been reported as a risk factor for vascular complications[6], [22], [24], this study investigated a novel quantitative method of measuring femoral plaque. Despite finding an association with necrotic core volume and VARC outcomes, we did not find a significant association between the volume of calcification and VARC composite outcome. A possible explanation for this finding may be that calcified plaque is a risk factor only if it is present on the anterior wall of the CFA and percutaneous closure was avoided in these patients. Another possibility is that the presence of calcified plaque acts as a surrogate for other plaque types, a feature seen in the coronaries[29]. The use of plaque map improves the classification of plaque composition and our study demonstrates a strong association between necrotic core and VARC outcomes (Odds Ratio 17.49), this suggests that common femoral artery plaque necrotic core may be a key predisposing factor to vascular complications.
Increased time to haemostasis was only associated with previous MI, and ProGlide® device closure in our study. This was in keeping with previous studies that had demonstrated that underlying coronary artery[30], and vascular[31], disease have previously been shown as risk factors for bleeding complications after TAVI. Time taken for haemostasis was likely shorter for MANTA® than ProGlide® due to intrinsic differences in the methods of deployment and the need for additional ProGlide® deployment in nine cases. Whilst the actual difference is time (4.3 seconds) is unlikely to be clinically relevant, the requirement for additional devices may have cost implications.

**Limitations**

There were some limitations to this study. Firstly, diagnosis of plaque composition in this study was only radiological, and was not supported by other means, such as intra-vascular imaging. However, our method has been utilised in previous work, which has demonstrated the suitability of CT imaging with attenuation ratios to classify different compositions of coronary plaque validated against the gold standard of post-mortem histology[25].

Secondly, the sheaths used for deployment of the Sapien 3 valve (Edwards Lifesciences) incorporate a dynamic expandable technology so the actual outer diameter will be larger than that stated following valve deployment[32]. Finally, patients with VCD closure were recruited for this study sequentially and therefore were not randomised. Therefore, despite the use of multivariate analysis, bias cannot be excluded in this study.

**Conclusion**

Computed tomography defined femoral artery plaque composition utilising plaque maps predicted vascular complications during transcatheter aortic valve implantation. Necrotic core, rather than calcified plaque volume was associated with a significant increase in VARC vascular complications along with increased sheath size.

**Declarations**

**CONFLICTS OF INTEREST**

There are no conflicts of interest for any authors relevant to this work.

**STUDY FUNDING**

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

**References**


Figures
Figure 1

Exclusion criteria

TAVI: transcatheter aortic valve implantation, CT: computed tomography
Figure 2

Plaque map analysis of common femoral artery

(A) Common femoral artery with predominantly non-calcified plaque.

(B) Plaque map analysis revealing necrotic core (red), fibrous plaque (blue) and lumen (green)

(C) Common femoral artery with predominantly calcified plaque

(D) Plaque map analysis revealing calcified plaque (yellow) and lumen (green)

Image not available with this version

Figure 3
VARC Vascular access and access-related complications. Adapted from Kappetein et al (2013)\textsuperscript{19}

*Refers to VARC bleeding definitions

**Supplementary Files**

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