Data on plug-based large-bore arteriotomy vascular closure device related access complications

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**A B S T R A C T**

This article provides supplementary tables and figures to the research article: Frequency, Impact and Predictors of Access Complications with Plug-Based Large-Bore Arteriotomy Closure - A patient level meta-analysis [1]. The data provide insight in the type and management of access complications related to the plug-based MANTA vascular closure device (VCD) for large-bore catheter-based cardiovascular interventions. Since MANTA is mostly used in transcatheter aortic valve replacement (TAVR) procedures, this article also contains a sub-group analysis on TAVR procedures using contemporary valve-platforms. Further, data describing MANTA hemostasis times and mortality causes are included. For this dataset, individual patient data were derived from a European and a North American device approval study (the Conformité Européenne [CE] mark study and the investigational device exemption SAFE-MANTA study [2,3]) in addition to a

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post-approval registry (the MARVEL registry [4]) covering a total of 891 patients who were enrolled between 2015 and 2019 across 28 investigational sites. Eligibility criteria were most stringent in the SAFE MANTA study (38% of patients) whereas the MARVEL registry applied liberal and only relative exclusion criteria (56% of patients). A total of 78 Roll-in cases (i.e. first or second time operator use of the MANTA VCD) who were excluded from analysis in SAFE MANTA were included in the present to evaluate a potential learning curve effect. Therefore, this dataset reflects the largest study population undergoing arteriotomy closure with the MANTA VCD by operators at various levels of experience, which can be valuable to further build on research regarding percutaneous large-bore arteriotomy management.

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**Specifications Table**

| Subject         | Cardiology and Cardiovascular Medicine |
|-----------------|----------------------------------------|
| Specific subject area | Large-bore catheter-based cardiac and vascular interventions |
| Type of data    | Tables and Figures                     |
| How data were acquired | In this patient-level meta-analysis, data were derived from two multicenter, prospective, single arm medical device approval studies (the CE mark study [2], and the Investigational Device Exemption SAFE-MANTA Pivotal Study [31]) in addition to a multicenter prospective post-approval study (the MANta Registry for Vascular Large-borE Closure [MARVEL] registry [4]). Statistical analyses were performed using Statistical Package for the Social Sciences version 25 (IBM, Armonk, New York) |
| Data format     | Analysed                               |
| Parameters for data collection | The one inclusion criterion in all studies was: all patients undergoing percutaneous cardiac interventions with large-bore catheter sizes and planned access closure using the MANTA VCD. Exclusion criteria in each of the three studies are detailed in Table 1. The main exclusion criteria were: |
| Description of data collection | All clinical data were prospectively collected and clinical follow-up was planned between 30- and 60 days after the procedure. An independent clinical research organization overlooked study conduction and monitoring. All vascular- and bleeding complications were adjudicated by independent clinical event committees. For the purpose of this patient-level meta-analysis, a selection of individual patient data were merged in a dedicated database and used for these analyses. |
| Data source location | Source location of CE-mark and SAFE-MANTA trial data: Teleflex Inc. Exton Pennsylvania United States of America Source location of MARVEL trial data: Erasmus Medical Center Rotterdam The Netherlands |
| Data accessibility | With the article |

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Value of the Data

- Vascular management in large-bore catheter-based interventions is challenging and affects patient outcome. These supplementary data provide detailed insight into the type and management of MANTA related access complications across various large-bore catheter-based interventions and also in a more homogenous population of patients undergoing TAVR using contemporary valves.
- The patients in this dataset reflect the largest study population undergoing arteriotomy closure with the MANTA VCD by operators at various levels of experience. It can be valuable to further build on research regarding large-bore arteriotomy management which ultimately benefits patients undergoing large-caliber catheter-based interventions.
- The data described should help understand the mechanisms of MANTA related access complications in patients undergoing various catheter-based interventions such as TAVR, which can be useful to optimize risk stratification, pre-procedural planning, vascular management and future iterations in (plug-based) closure technologies.

1. Data Description

This dataset provides relevant details on the frequency, impact and predictors of MANTA related access complications. Data are presented in Tables and Figures. Table 1 describes the general characteristics of each of the three studies from which data were used for the present dataset. Each study had a prospective, observational, multicenter design with similar inclusion criteria but various exclusion criteria. Table 2 provides raw data on the type, management and outcome of access complications of the entire cohort. The frequency of major / minor access complications was 9%; life-threatening bleeding occurred in 0.4% and mortality in 0.1% (i.e. 1 case of an arterial rupture). In Table 3, the data are summarized for the subgroup of TAVR procedures in which the Sapien S3 / Ultra or Evolut Pro-valve was used (i.e. the two most commonly used valves in contemporary practice). The frequency of major / minor access complications was 10% in the TAVR-group and none of the access complications in TAVR were associated with life-threatening bleeding or death. The main article demonstrated that the frequency of access complications in Roll-in cases (first or second time operator use of MANTA) was similar as compared to non-Roll-in cases (third time or more operator experience with MANTA). Table 4 demonstrates that this finding was despite the fact that Roll-in cases as a group had higher STS score as compared to patients not labelled as a Roll-in case (median STS score: 3.8 vs. 3.1%, respectively, p = 0.015). Fig. 1 demonstrates the MANTA VCD hemostasis times: 67% of patients had complete hemostasis within 1 min and 88% within 5 min. Because device profile determines arteriotomy size and complication risk, access complication frequencies were further stratified per valve-platform as shown in Fig. 2. It was found that the valve-platform exhibiting the smallest device profile (Evolut R) was associated with access complications in 7.1% while other (larger profile) valve-platforms were associated with complication rates between 8.3 and 13.1%.

2. Experimental Design, Materials and Methods

As mentioned above, this patient-level meta-analysis pooled data from two medical device approval studies and one post-approval registry to assess the frequency, impact and
| Study name                | Design                                | Registration                        | Time period        | Investigational sites | No. of patients enrolled, total | No. of patients enrolled, Roll-in cases | No. of operators | Independent clinical event committee | Data safety and monitoring                                                                 |
|--------------------------|---------------------------------------|-------------------------------------|--------------------|-----------------------|-------------------------------|----------------------------------------|-----------------|-------------------------------------|-----------------------------------------------------------------------------------------|
| CE Mark Study            | Prospective, single arm, multicenter  | NCT02521948 (study for CE mark approval) | Jul-2015–Jan-2016  | 3 in Europe           | 50                            | 0                                      | 9               | yes                                 | 100% of data monitored by Factory-CRO (Bilthoven, the Netherlands)                     |
| SAFE Manta US Pivotal Study (PSD-19) | Prospective, single arm, multicenter  | G160115 (study for FDA approval)   | Nov-2016–Sep 2017 | 19 in United States, 1 in Canada | 341                           | 78                                      | 42              | yes                                 | 100% event adjudication by Baim Institute for Clinical Research (Boston, MA); 100% of data monitored by Health Policy Associates Inc. |
| MARVEL                   | Prospective, single arm, multicenter  | NCT03330002 (Post market study)   | Feb-2018–Jul 2019  | 9 in Europe, 1 in Canada | 500                           | 0                                      | 31              | yes                                 | 30% of data monitored by Factory-CRO (Bilthoven, the Netherlands)                     |

**Inclusion Criteria**
- Candidate for elective percutaneous interventional procedure with 12-F to 19F catheter size (sheath outer diameter 16-F to 24.5F)
- CFA diameter ≥5 mm for 14-F MANTA and ≥6 mm for 18-F Manta
- Age ≥21 years

**Exclusion Criteria**
- Arterial puncture outside CFA
- CFA size inappropriate for selected sheath size
- Complicated CFA access (i.e., excessive hematoma surrounding puncture site, arteriovenous fistula, posterior wall puncture)
- Significant anemia (Hb < 10 g/dL or Ht <30%)
- Morbid obesity or cachexia (body mass index >40 kg/m² or <20 kg/m²)
- Known bleeding disorder
- Excessive calcification of the access vessel
- Severe peripheral artery disease precluding safe introduction of a large arterial sheath
- Marked tortuosity of the femoral or iliac artery

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| Mieghem et al. JACC Cardiovasc. Interv 2017 | Wood et al. Circ Cardiovasc. Interv 2019 | Kroon et al. Cath Cardiovasc. Interv. 2020 |
|------------------------------------------------|------------------------------------------------|------------------------------------------------|
| Renal insufficiency (serum creatinine >2.5 mg/dl) | CFA excessive calcium precluding safe access in the opinion of the operator or severe peripheral vascular disease (on CT-A) | Morbid obesity or cachexia (body mass index >40 kg/m² or <20 kg/m²) |
| Inability to ambulate at baseline | Recent (<14 days) femoral artery puncture, incomplete healing of recent femoral artery puncture | Baseline systolic blood pressure >180 mmHg |
| | Left ventricular ejection fraction <20% | | |
| | Renal insufficiency (serum creatinine >2.5 mg/dl) or on dialysis | | |
| | Puncture site other than the CFA (i.e. profunda femoral artery, superficial femoral artery or at bifurcation of these arteries) | | |
| | Marked tortuosity of femoral or iliac artery | | |
| | Intraprocedural complications at femoral access site around the large bore sheath (i.e. angiographic evidence of thrombus or injury) | | |
| | Activated clotting time > 250 s before removal of the sheath | | |
| | Systolic blood pressure > 180 mmHg or diastolic >110 mmHg | | |

**Abbreviations:** CFA, common femoral artery; F, French; Hb, hemoglobin; Ht, hematocrit.

* Some investigational sites and operators participated in >1 study.

* Roll in cases were executed by operators with first or second time use of the MANTA vascular closure device, of which 78 cases stem from the SAFE MANTA study that were not included in the original trial.
| Case | Valve-platform (in case of TAVR) | Access complication details | Treatment | No. blood transfusions | Timing of complication (days after procedure) | Access complication (major or minor) | Bleeding complication (life-threatening/disabling or major) |
|------|----------------------------------|-----------------------------|-----------|------------------------|---------------------------------------------|-----------------------------------|---------------------------------|
| 1    | Sapien 3 / Ultra                 | stenosis                    | stent     | 0                      | 0                                           | major                            | no                              |
| 2    | Sapien 3 / Ultra                 | incomplete arteriotomy closure | compression | 0                      | 1                                           | major                            | major                           |
| 3    | Evolut R                         | incomplete arteriotomy closure | Ethanol blood patch injection in inferior epigastric artery | 3                      | 6                                           | major                            | major                           |
| 4    | Evolut PRO                       | occlusion                   | balloon   | 0                      | 0                                           | major                            | no                              |
| 5    | Sapien 3 / Ultra                 | stenosis                    | stent     | 0                      | 0                                           | major                            | no                              |
| 6    | Sapien 3 / Ultra                 | thrombotic occlusion        | surgical repair | 0                      | 0                                           | major                            | no                              |
| 7    | Evolut PRO                       | occlusion                   | surgical repair | 0                      | 0                                           | major                            | no                              |
| 8    | Sapien 3 / Ultra                 | occlusion                   | balloon   | 0                      | 0                                           | major                            | major                           |
| 9    | n.a. (EVAR)                      | thrombotic occlusion        | stent     | 0                      | 0                                           | major                            | no                              |
| 10   | Sapien 3 / Ultra                 | incomplete arteriotomy closure | stent     | 0                      | 0                                           | major                            | no                              |
| 11   | Sapien 3 / Ultra                 | thrombotic occlusion        | balloon   | 0                      | 0                                           | major                            | no                              |
| 12   | Sapien 3 / Ultra                 | incomplete arteriotomy closure | compression | 1                      | 0                                           | minor                            | major                           |
| 13   | Evolut R                         | incomplete arteriotomy closure | none     | 0                      | 1                                           | minor                            | major                           |
| 14   | Evolut R                         | incomplete arteriotomy closure | none     | 0                      | 1                                           | minor                            | major                           |
| 15   | Sapien 3 / Ultra                 | pseudoaneurysm              | compression | 0                      | 0                                           | minor                            | no                              |
| 16   | Sapien 3 / Ultra                 | pseudoaneurysm              | none      | 0                      | 1                                           | minor                            | no                              |
| 17   | Sapien 3 / Ultra                 | pseudoaneurysm              | none      | 0                      | 1                                           | minor                            | no                              |
| 18   | Evolut R                         | pseudoaneurysm              | compression | 0                      | 1                                           | minor                            | no                              |

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| Case | Valve-platform (in case of TAVR) | Access complication details | Treatment | No. blood transfusions | Timing of complication (days after procedure) | Access complication (major or minor) | Bleeding complication (life-threatening/disabling or major) |
|------|----------------------------------|-----------------------------|-----------|-----------------------|---------------------------------------------|-----------------------------------|--------------------------------------------------|
| 19   | Evolut PRO                        | nerve injury                | none      | 0                     | 0                                          | minor                             | no                                               |
| 20   | n.a. (EVAR)                       | pseudoaneurysm              | none      | 0                     | 27<sup>a</sup>                             | minor                             | no                                               |
| 21   | n.a. (EVAR)                       | pseudoaneurysm              | compression | 0                     | 1                                          | minor                             | no                                               |
| 22   | Sapien 3 / Ultra                  | pseudoaneurysm              | none      | 0                     | 57<sup>a</sup>                             | minor                             | no                                               |
| 23   | n.a. (EVAR)                       | pseudoaneurysm              | none      | 0                     | 41<sup>a</sup>                             | minor                             | no                                               |
| 24   | Sapien 3 / Ultra                  | thrombotic occlusion        | balloon   | 0                     | 0                                          | major                             | no                                               |
| 25   | Sapien 3 / Ultra                  | stenosis                    | none      | 1                     | 0                                          | major                             | no                                               |
| 26   | Sapien 3 / Ultra                  | dissection                  | balloon   | 0                     | 0                                          | major                             | no                                               |
| 27   | Sapien 3 / Ultra                  | occlusion                   | surgical repair | 1                     | 0                                          | major                             | no                                               |
| 28   | Sapien 3 / Ultra                  | occlusion                   | surgical repair | 0                     | 0                                          | major                             | no                                               |
| 29   | Sapien 3 / Ultra                  | occlusion                   | surgical repair | 0                     | 0                                          | major                             | no                                               |
| 30   | Sapien 3 / Ultra                  | stenosis                    | stent     | 0                     | 0                                          | minor                             | no                                               |
| 31   | Evolut R                          | pseudoaneurysm              | compression | 0                     | 1                                          | minor                             | no                                               |
| 32   | n.a. (EVAR)                       | pseudoaneurysm              | none      | 0                     | 34<sup>a</sup>                             | minor                             | no                                               |
| 33   | Sapien 3 / Ultra                  | thrombotic occlusion        | surgical repair | 0                     | 0                                          | major                             | no                                               |
| 34   | Sapien 3 / Ultra                  | incomplete arteriotomy closure | surgical repair | 2                     | 0                                          | major                             | major                                            |
| 35   | Sapien 3 / Ultra                  | thrombotic occlusion        | none      | 0                     | 0                                          | major                             | no                                               |
| 36   | Evolut PRO                        | incomplete arteriotomy closure | surgical repair | 2                     | 0                                          | major                             | no                                               |
| 37   | Evolut PRO                        | pseudoaneurysm              | stent     | 2                     | 0                                          | major                             | major                                            |
| 38   | Evolut PRO                        | incomplete arteriotomy closure | none      | 0                     | 0                                          | major                             | no                                               |
| 39   | Accurate Neo                      | pseudoaneurysm              | balloon   | 2                     | 0                                          | major                             | major                                            |
| 40   | n.a. (EVAR)                       | incomplete arteriotomy closure | surgical repair | 0                     | 0                                          | major                             | major                                            |
| 41   | Evolut PRO                        | incomplete arteriotomy closure | surgical repair | 2                     | 0                                          | major                             | no                                               |
| 42   | Evolut R                          | incomplete arteriotomy closure | stent     | 4                     | 0                                          | major                             | life-threatening/disabling                      |

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| Case | Valve-platform (in case of TAVR) | Access complication details | Treatment | No. blood transfusions | Timing of complication (days after procedure) | Access complication (major or minor) | Bleeding complication (life-threatening/disabling or major) |
|------|---------------------------------|-----------------------------|------------|------------------------|-----------------------------------------------|--------------------------------------|----------------------------------------------------------|
| 43   | Evolut PRO                      | dissection                  | surgical repair | 0                      | 0                                             | major                                | no                                                       |
| 44   | Evolut PRO                      | dissection                  | surgical repair | 0                      | 0                                             | major                                | no                                                       |
| 45   | Sapien 3 / Ultra                | thrombotic occlusion        | surgical repair | 0                      | 0                                             | major                                | no                                                       |
| 46   | n.a. (aortic valvuloplasty)     | incomplete arteriotomy closure | surgical repair | 2                      | 0                                             | major                                | life-threatening/disabling                            |
| 47   | Sapien 3 / Ultra                | incomplete arteriotomy closure | balloon      | 2                      | 0                                             | major                                | major                                                   |
| 48   | Accurate Neo                    | stenosis                    | surgical repair | 3                      | 0                                             | major                                | life-threatening/disabling                          |
| 49   | Evolut R                        | incomplete arteriotomy closure | surgical repair | 8                      | 0                                             | major                                | life-threatening/disabling                          |
| 50   | Accurate Neo                    | incomplete arteriotomy closure | surgical repair | 3                      | 0                                             | major                                | major                                                   |
| 51   | Evolut PRO                      | incomplete arteriotomy closure | compression   | 0                      | 0                                             | major                                | major                                                   |
| 52   | Sapien 3 / Ultra                | stenosis                    | stent        | 0                      | 0                                             | major                                | no                                                      |
| 53   | Sapien 3 / Ultra                | dissection                  | compression   | 0                      | 0                                             | minor                                | no                                                      |
| 54   | Evolut PRO                      | dissection                  | balloon       | 0                      | 0                                             | minor                                | no                                                      |
| 55   | Evolut PRO                      | dissection                  | stent         | 0                      | 0                                             | minor                                | no                                                      |
| 56   | Evolut PRO                      | dissection                  | none          | 0                      | 0                                             | minor                                | no                                                      |
| 57   | Sapien 3 / Ultra                | dissection                  | none          | 0                      | 0                                             | minor                                | no                                                      |
| 58   | Sapien 3 / Ultra                | dissection                  | compression   | 0                      | 0                                             | minor                                | no                                                      |
| 59   | Evolut PRO                      | dissection                  | none          | 0                      | 0                                             | minor                                | no                                                      |
| 60   | Evolut PRO                      | dissection                  | stent         | 0                      | 0                                             | minor                                | no                                                      |
| 61   | Accurate Neo                    | dissection                  | stent         | 0                      | 0                                             | minor                                | no                                                      |
| 62   | Sapien 3 / Ultra                | stenosis                    | compression   | 0                      | 0                                             | minor                                | no                                                      |
| 63   | Sapien 3 / Ultra                | stenosis                    | balloon       | 0                      | 0                                             | minor                                | no                                                      |
| 64   | Evolut PRO                      | stenosis                    | surgical repair | 0                      | 0                                             | minor                                | no                                                      |
| 65   | Evolut PRO                      | pseudoaneurysm              | none          | 0                      | 1                                             | minor                                | no                                                      |
| 66   | Sapien 3 / Ultra                | pseudoaneurysm              | none          | 0                      | 0                                             | minor                                | no                                                      |
| 67   | Evolut R                        | pseudoaneurysm              | compression   | 0                      | 0                                             | minor                                | no                                                      |
| 68   | Evolut R                        | pseudoaneurysm              | lidocaine/epinephrine injection | 0                      | 0                                             | minor                                | no                                                      |

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| Case | Valve-platform (in case of TAVR) | Access complication details | Treatment | No. blood transfusions | Timing of complication (days after procedure) | Access complication (major or minor) | Bleeding complication (life-threatening/disabling or major) |
|------|---------------------------------|----------------------------|-----------|------------------------|-----------------------------------------------|---------------------------------------|--------------------------------------------------|
| 69   | Sapien 3 / Ultra                | pseudoaneurysm             | lidocaine/epinephrine combination or thrombin injection | 1                      | 1                                      | minor                                         | no                                               |
| 70   | Accurate Neo                    | pseudoaneurysm             | balloon   | 0                      | 0                                      | minor                                         | no                                               |
| 71   | Accurate Neo                    | pseudoaneurysm             | balloon   | 0                      | 0                                      | minor                                         | no                                               |
| 72   | Sapien 3 / Ultra                | incomplete arteriotomy closure | compression | 0                      | 0                                      | minor                                         | no                                               |
| 73   | Sapien 3 / Ultra                | incomplete arteriotomy closure | lidocaine/epinephrine combination or thrombin injection | 0                      | 0                                      | minor                                         | no                                               |
| 74   | Sapien 3 / Ultra                | incomplete arteriotomy closure | lidocaine/epinephrine combination or thrombin injection | 0                      | 0                                      | minor                                         | no                                               |
| 75   | Sapien 3 / Ultra                | incomplete arteriotomy closure | lidocaine/epinephrine combination or thrombin injection | 0                      | 0                                      | minor                                         | no                                               |
| 76   | Sapien 3 / Ultra                | incomplete arteriotomy closure | compression | 0                      | 1                                      | minor                                         | no                                               |
| 77   | Sapien 3 / Ultra                | incomplete arteriotomy closure | surgical repair | 0                      | 0                                      | minor                                         | no                                               |
| 78   | Sapien 3 / Ultra                | incomplete arteriotomy closure | stent    | 0                      | 0                                      | minor                                         | no                                               |
| 79   | Sapien 3 / Ultra                | incomplete arteriotomy closure | none     | 0                      | 0                                      | minor                                         | no                                               |
| 80   | Evolut PRO                      | incomplete arteriotomy closure | balloon   | 0                      | 0                                      | minor                                         | no                                               |
| 81   | Sapien 3 / Ultra                | incomplete arteriotomy closure | surgical repair | 0                      | 0                                      | major                                          | major                                            |

Abbreviations: EVAR, endovascular aortic repair; TAVR, transcatheter aortic valve replacement.

a Complication diagnosed after discharge from primary hospital admission.

b Complication leading to death.
Table 3
Subgroup analysis of access complications and management in patients undergoing TAVR with SapienS3 / Ultra or Evolut PRO valves.

| Table 3 | Subgroup analysis of access complications and management in patients undergoing TAVR with SapienS3 / Ultra or Evolut PRO valves. |
|---------|----------------------------------------------------------------------------------------------------------------------------------|
| Access complications |                                                                                                                                  |
|           | minor  | major  | all     |
| n = 29 (5.0%)a | n = 30 (5.2%)b | n = 59 (10.2%)a |
| **Type of vascular injury** |                                                                                                                                  |
| Incomplete arteriotomy closure | 11 (1.9) | 9 (1.6) | 20 (3.4) |
| Dissection | 8 (1.4) | 3 (0.5) | 11 (1.9) |
| Stenosis | 3 (0.5) | 5 (0.9) | 8 (1.4) |
| Occlusion | 0 | 12 (2.1) | 12 (2.1) |
| Pseudo-aneurysm | 6 (1.0) | 1 (0.2) | 7 (1.2) |
| Transient nerve injury | 1 (0.2) | 0 | 1 (0.2) |
| **Treatment** |                                                                                                                                  |
| Surgical repair | 2 (0.3) | 13 (2.2) | 15 (2.6) |
| Stenting | 3 (0.5) | 6 (1.0) | 9 (1.6) |
| Prolonged balloon inflation | 3 (0.5) | 6 (0.8) | 9 (1.6) |
| None / manual compression | 17 (2.9) | 5 (0.7) | 22 (3.8) |
| Percutaneous injectionb | 4 (0.7) | 0 | 4 (0.7) |
| **Bleeding complications** |                                                                                                                                  |
| Life-threatening or disabling | 0 | 0 | 0 |
| Major | 0 | 9 (1.6) | 9 (1.6) |

a Data are presented as n (%), out of a total of 580 patients treated with Edwards Sapien S3 / Ultra or Evolut PRO valves).
b All patients underwent thrombin or lidocaine injection, except one patient who underwent ethanol injection in the inferior epigastric artery.

Table 4
Baseline and peri-procedural characteristics stratified according to Roll-in case.

| Characteristic | Total | No Roll-in casea | Roll-in casea | p-value |
|---------------|-------|-----------------|---------------|---------|
|               | N = 891 | N = 813 | N = 78   |         |
| **Baseline characteristics** | | | | |
| Age, mean (SD), y | 80 (8) | 80 (7) | 78 (10) | 0.004 |
| Female gender | 364 (41) | 346 (43) | 18 (23) | 0.001 |
| Body mass index, median (IQR), kg/m² | 27 (24–30) | 27 (24–30) | 28 (25–32) | 0.057 |
| Peripheral vascular disease | 91 (10) | 76 (9) | 15 (19) | 0.006 |
| Previous coronary artery bypass graft | 126 (14) | 104 (13) | 22 (28) | <0.001 |
| Previous percutaneous coronary intervention | 263 (30) | 239 (29) | 24 (31) | 0.80 |
| Previous cerebrovascular event | 94 (11) | 94 (12) | 0 | <0.001 |
| Permanente pacemaker | 87 (10) | 75 (9) | 12 (15) | 0.080 |
| Glomerular filtration rate < 60 mL/min | 453 (51) | 409 (50) | 44 (56) | 0.31 |
| Society of Thoracic Surgeons' score, median (IQR), % | 3.2 (2.1–4.9) | 3.1 (2.1–4.7) | 3.8 (2.5–5.5) | 0.015 |
| Oral anticoagulant | 199 (22) | 190 (23) | 9 (12) | 0.017 |
| New oral anticoagulant | 87 (10) | 84 (10) | 3 (4) | 0.072 |
| **Procedural characteristics** | | | | |
| Activated clotting time before closure, median (IQR), sec | 175 (142–217) | 172 (142–218) | 190 (156–213) | 0.23 |
| Systolic blood pressure before closure, mean (SD), mmHg | 132 (23) | 132 (23) | 124 (20) | 0.001 |
| Protamine used before closure | 592 (66) | 531 (65) | 61 (78) | 0.021 |
| Procedure duration, median (IQR), min | 65 (48–87) | 64 (46–85) | 75 (56–101) | 0.004 |
| Time to haemostasis, median (IQR), sec | 31 (17–76) | 32 (17–83) | 27 (20–45) | 0.55 |
| **Post Procedural characteristics** | | | | |
| Length of stay, median (IQR), days | 2 (1–5) | 3 (2–5) | 2 (1–2) | <0.001 |

a Roll-in case indicates an operator first or second time use of the MANTA vascular closure device. Roll-in cases were excluded in the Device Exemption Primary Analysis Cohort of the SAFE MANTA study.

Predictors of MANTA related access complications after large-bore catheter-based cardiovascular interventions. Procedures were performed by 71 operators at 28 sites between 2015 and 2019. Table 1 describes all in- and exclusion criteria of each of the 3 studies from which data were derived. Overall, patients were eligible if they underwent percutaneous cardiovascular interventions and planned access closure using the MANTA VCD. Exclusion criteria were most stringent
in the SAFE MANTA trial, followed by the CE mark study whereas MARVEL applied liberal and only relative exclusion criteria. The most important exclusion criteria were morbid obesity or cachexia (body mass index >40 or <20 kg/m²), excessive femoral calcium or severe peripheral vascular disease, marked tortuosity of the iliofemoral tract and puncture site other than the common femoral artery. Of note, in SAFE MANTA poor left ventricular function and severe renal dysfunction were also exclusion criteria. In all patients, major and minor access complications were defined according to the updated Valve Academic Research Consortium 2 criteria [5]. All events were adjudicated by independent clinical event committees. A detailed description of the study population, MANTA device, the percutaneous procedures, iliofemoral data and clinical outcome assessment is presented in the main article [1]. Continuous variables were compared using the Student t-test or Mann Whitney U test when appropriate. Categorical variables are presented as numbers and percentages of patients and categorical variables were compared with the Chi square test. A two-sided \( p < 0.05 \) was considered to indicate significance. Statistical analyses were performed using Statistical Package for the Social Sciences version 25 (IBM, Armonk, New York).

**Ethics Statement**

Informed consent was obtained from all patients that were enrolled with the use of a prespecified patient information form. The herein reported data were derived from the SAFE-MANTA study (protocol identifier: PSD-109), CE-Mark study (protocol identifier: PSD-051) and
MARVEL registry (protocol identifier: PSD-212), and study protocols were approved by the Ethics Committees of each participating center.

CRediT Author Statement

Rutger-Jan Nuis: Conceptualization, Methodology, Formal analysis, Investigation, Data Curation, Visualization, Writing – Original Draft; David Wood: Conceptualization, Writing - Review & Editing; Herbert Kroon: Writing - Review & Editing; Maarten van Wiechen: Writing - Review & Editing; Darra Bigelow: Writing - Review & Editing; Chris Buller: Writing - Review & Editing; Joost Daemen: Writing - Review & Editing; Peter de Jaegere: Writing - Review & Editing; Zvonimir Krajcer: Writing - Review & Editing; John Webb: Writing - Review & Editing; Nicolas Van Mieghem: Conceptualization, Methodology, Writing - Review & Editing.

Declaration of Competing Interest

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