Supplemental Materials

Supplemental Methods

Search Strategy

Four databases (Medline, Embase, Web of Science and the Cochrane Library) were searched up to November 2020 using the following terms: (Transcatheter aortic valve implantation (TAVI) OR Transcatheter Aortic Valve Replacement (TAVR) OR Percutaneous aortic valve replacement/ implantation) AND (femoral artery OR transfemoral) AND (Ultrasonography OR echography OR fluoroscopy OR angiography). The detailed search strategy used is also shown on PROSPERO (CRD42020218259). The resultant titles and abstracts of the search were screened by three reviewers (JJHB, SR and RAK) for relevance. Then full texts were assessed for eligibility (Figure 1).

| | Medline | |
|----|--|-------|
| 1 | exp transcatheter aortic valve implantation/ | 6107 |
| 2 | Transcatheter aortic valve implantation.ti,ab. | 5211 |
| 3 | TAVI.ti,ab. | 4225 |
| 4 | exp Transcatheter Aortic Valve Replacement/ | 6107 |
| 5 | Transcatheter aortic valve replacement.ti,ab. | 4439 |
| 6 | TAVR.ti,ab. | 3363 |
| 7 | Percutaneous aortic valve replacement.ti,ab. | 189 |
| 8 | percutaneous aortic valve implantation.ti,ab. | 118 |
| 9 | 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 | 11826 |
| 10 | exp Femoral Artery/ | 28820 |
| 11 | femoral artery.ti,ab. | 17734 |
| 12 | transfemoral.ti,ab. | 5460 |
| 13 | 10 or 11 or 12 | 42287 |

Detailed search strategy

| 14 | exp Ultrasonography/ or (ultrasound or ultrason* or echograph*).ti,ab. | 635204 |
|----|--|---------|
| 15 | exp fluoroscopy/ or fluoroscop*.ti,ab. | 39546 |
| 16 | exp angiography/ or angiog*.ti,ab. | 452324 |
| 17 | 14 or 15 or 16 | 1070170 |
| 18 | 9 and 13 and 17 | 513 |

| | Embase | |
|----|--|---------|
| 1 | exp transcatheter aortic valve implantation/ | 22618 |
| 2 | Transcatheter aortic valve implantation.ti,ab. | 9897 |
| 3 | TAVI.ti,ab. | 10090 |
| 4 | exp Transcatheter Aortic Valve Replacement/ | 22618 |
| 5 | Transcatheter aortic valve replacement.ti,ab. | 7953 |
| 6 | TAVR.ti,ab. | 7210 |
| 7 | Percutaneous aortic valve replacement.ti,ab. | 329 |
| 8 | percutaneous aortic valve implantation.ti,ab. | 218 |
| 9 | 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 | 25520 |
| 10 | exp Femoral Artery/ | 34463 |
| 11 | femoral artery.ti,ab. | 25720 |
| 12 | transfemoral.ti,ab. | 9367 |
| 13 | 10 or 11 or 12 | 50752 |
| 14 | exp Ultrasonography/ or (ultrasound or ultrason* or echograph*).ti,ab. | 1091052 |
| 15 | exp fluoroscopy/ or fluoroscop*.ti,ab. | 66362 |
| 16 | exp angiography/ or angiog*.ti,ab. | 638256 |
| 17 | 14 or 15 or 16 | 1673462 |
| 18 | 9 and 13 and 17 | 1720 |

Cochrane Library

| ID | Search Hits | |
|-----|---|-----|
| #1 | MeSH descriptor: [Transcatheter Aortic Valve Replacement] explode all trees | 150 |
| #2 | "Transcatheter aortic valve implantation" 635 | |
| #3 | TAVI 381 | |
| #4 | ("Transcatheter aortic valve replacement"):ti,ab,kw 490 | |
| #5 | TAVR 433 | |
| #6 | "Percutaneous aortic valve replacement" 1 | |
| #7 | "percutaneous aortic valve implantation" 7 | |
| #8 | (2-#7) 918 | |
| #9 | MeSH descriptor: [Femoral Artery] explode all trees 991 | |
| #10 | "femoral artery" 2214 | |
| #11 | transfemoral 612 | |
| #12 | (3-#11) 2680 | |
| #13 | MeSH descriptor: [Ultrasonography] explode all trees 13623 | |
| #14 | (ultrasound or ultrason* or echograph*)44573 | |
| #15 | MeSH descriptor: [Fluoroscopy] explode all trees 627 | |
| #16 | fluoroscop* 3483 | |
| #17 | MeSH descriptor: [Angiography] explode all trees 7178 | |
| #18 | angiog*23923 | |
| #19 | {OR #13-#18} 73402 | |
| #20 | (4, #12, #19) 50 | |

Web of Science

| #9 | <u>193</u> | #8 AND #5 AND #4 |
|----|----------------|--|
| | | Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI- SSH, ESCI Timespan=All years |
| #8 | <u>693,190</u> | #7 OR #6 |

| | | Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI- |
|----|----------------|--|
| | | SSII, ESCI Timespan-Ait years |
| #7 | <u>298,600</u> | ((TS=(fluoroscop* OR |
| | | angiog*))) AND DOCUMENT TYPES: (Article) |
| | | Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI- |
| | | SSH, ESCI Timespan=All years |
| #6 | 415,203 | ((TS=(ultrasound OR ultrason* OR |
| | | echograph*))) AND DOCUMENT TYPES: (Article) |
| | | Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI- |
| | | SSH, ESCI Timespan=All years |
| #5 | 17,479 | ((TS=("Femoral Artery" OR |
| | | "transfemoral"))) AND DOCUMENT TYPES: (Article) |
| | | Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI- |
| | | SSH, ESCI Timespan=All years |
| #4 | <u>6,771</u> | #3 OR #2 OR #1 |
| | | Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI- |
| | | SSH, ESCI Timespan=All years |
| #3 | <u>212</u> | ((TS=("Percutaneous aortic valve replacement" OR |
| | | "percutaneous aortic valve |
| | | implantation"))) AND DOCUMENT TYPES: (Article) |
| | | Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI- |
| | | SSH, ESCI Timespan=All years |
| #2 | <u>3,155</u> | ((TS=("Transcatheter Aortic Valve Replacement" OR |
| | | "TAVR"))) AND DOCUMENT TYPES: (Article) |
| | | Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI- |
| | | SSH, ESCI Timespan=All years |
| #1 | <u>4,326</u> | ((TS=("Transcatheter aortic valve implantation" OR |
| | | "TAVI"))) AND DOCUMENT TYPES: (Article) |
| | | Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI- |
| | | SSH, ESCI Timespan=All years |
| | | |

Data extraction

Study design and patient characteristics were derived and input in abbreviated summary into tables. Where not explicitly stated, range of sheath sizes were estimated from reported valve type and size. Outcomes were transferred in the form of crude dichotomous events. Studies that controlled for multiple confounders were extracted in the form of adjusted odds ratios (ORs) and standard errors calculated from 95% confidence intervals (95% CIs) or as event rates in propensity-matched studies. Where data on total complication rates was not provided, it was calculated by combining major and minor rates.

Supplemental Tables

Table I. Study participant characteristics

| Study | Comparison arms | Average age (years) | Female sex (%) | PAD (%) | Diabetes (%) | Risk score | Antiplate lets | Anticoag ulants |
|------------------------------------|---------------------------|------------------------|-------------------|------------|-----------------|-----------------------|-------------------|--------------------|
| (first author, year) | | | | | | | (%) | (%) |
| Kotronias 2020 ¹⁷ | Total | 83 (79-86) | 45.2 | 47.2 | 26.8 | - | - | - |
| Potluri 2020 ¹⁹ | Ultrasound | 82 (53.8- 100.8) | 50.0 | 24.5 | 42.6 | STS: 5.6 | - | - |
| | Fluoroscopy | 84.1 (58.6-95.2) | 40.9 | 27.2 | 36.2 | STS: 6.4 | - | - |
| Vincent 2020 ⁷ | Ultrasound | 82.1 (6.9) | 62.1 | 34.7 | 32.6 | STS: 5.4 | 31.6 | 30.5 |
| vincent 2020 | Fluoroscopy | 81.7 (5.4) | 56.8 | 31.6 | 29.5 | STS: 5.3 | 32.6 | 25.3 |
| Witberg 2020 ²¹ | Ultrasound | 82.3 (7.0) | 54.3 | 13.0 | 25.5 | Euro: 23.7 | 64.3 | 39.6 |
| | Fluoroscopy | 81.7 (8.6) | 53.3 | 12.0 | 25.0 | Euro: 22.3 | 64.4 | 38.0 |
| Bouteau 2019 ^{14,15} | Ultrasound | 83.8 (6.6) | 46.4 | 5.6 | 32.9 | STS:4.3 Euro 4.6 | - | 35.0 |
| | Fluoroscopy | 84.9 (5.7) | 48.6 | 6.8 | 27.5 | STS: 4.7 Euro: 6.4 | - | 32.9 |
| Moriyama 2019 ¹⁸ | Total | - | - | - | - | - | - | - |
| Khan 2019 ¹⁷ | Total | - | - | - | - | - | - | - |
| Elbaz-Greener 2017 ⁶ | Ultrasound Fluoroscopy | 83 (79-87) | 46.5 | 16.5 | 28.9 | STS: 6.1 STS: 7.9 | 79.3 | 32.6 |

Antiplatelet therapy refers to single or dual antiplatelet therapy. Euro: Logistic EuroSCORE II; STS: The Society of Thoracic Surgeons Score; PAD: peripheral arterial disease.

 Table II. Risk of bias assessment of outcomes according to ROBINS-I (Risk Of Bias In Non-randomised Studies of Interventions)

| First author, Year (Ref. #) | Bias due to confounding | Bias in selection of participants | Bias in classification of interventions | Bias due to departures from intended interventions | as due to Bias in Selection Selection of outcomes reported results | | Bias in selection of reported results | Overall risk of bias judgment |
|----------------------------------|----------------------------|---|---|---|--|----------------|--|----------------------------------|
| | | М | ajor and minor ac | cess site vascular (| complications | | | |
| Kotronias, 2020 ¹⁷ | Moderate | Low | Low | Low | Low | Moderate | Low | Moderate |
| Potluri, 2020 ¹⁹ | Serious | Low | Low | Low | No information | Low | Low | Serious |
| Vincent, 2020 ⁷ | Moderate | Low | Low | Low | Low | Moderate | Low | Moderate |
| Witberg, 2020 ²¹ | Moderate | Low | Low | Low | No information | Moderate | Low | Moderate |
| Bouteau, 2019 ^{14,15} | Serious | Low | Low | Low | Low | Low | Low | Serious |
| Moriyama, 2019 ¹⁸ | Moderate | Low | Low | Low | No information | No information | No information | Moderate |
| Elbaz-Greener, 2017 ⁶ | Serious | Low | Low | Low | Low | Moderate | Low | Serious |
| | | | Major access si | ite vascular compl | ications | | | |
| Kotronias, 2020 ¹⁷ | Moderate | Low | Low | Low | Low | Moderate | Low | Moderate |
| Potluri, 2020 ¹⁹ | Serious | Low | Low | Low | No information | Low | Low | Serious |
| Vincent, 2020 ⁷ | Moderate | Low | Low | Low | Low | Moderate | Low | Moderate |
| Witberg, 2020 ²¹ | Moderate | Low | Low | Low | No information | Moderate | Low | Moderate |
| Bouteau, 2019 ^{14,15} | Serious | Low | Low | Low | Low | Low | Low | Serious |
| Moriyama, 2019 ¹⁸ | Moderate | Low | Low | Low | No information | No information | No information | Moderate |

| Khan, 2019 ¹⁶ | Serious | No information | Low | Low | No information | No information | No information | Serious |
|----------------------------------|----------|----------------|--------------------|----------------------|-------------------|----------------|----------------|----------|
| Elbaz-Greener, 2017 ⁶ | Serious | Low | Low | Low | Low | Moderate | Low | Serious |
| | | | Minor access si | ite vascular compl | ications | | | |
| Kotronias, 2020 ¹⁷ | Moderate | Low | Low | Low | Low | Moderate | Low | Moderate |
| Potluri, 2020 ¹⁹ | Serious | Low | Low | Low | No information | Low | Low | Serious |
| Vincent, 2020 ⁷ | Moderate | Low | Low | Low | Low | Moderate | Low | Moderate |
| Witberg, 2020 ²¹ | Moderate | Low | Low | Low | No information | Moderate | Low | Moderate |
| Bouteau, 2019 ^{14,15} | Serious | Low | Low | Low | Low | Low | Low | Serious |
| Moriyama, 2019 ¹⁸ | Moderate | Low | Low | Low | No information | No information | No information | Moderate |
| Elbaz-Greener, 2017 ⁶ | Serious | Low | Low | Low | Low | Moderate | Low | Serious |
| | | Life-threat | ening, major and 1 | ninor access site b | leeding complicat | tions | | |
| Kotronias, 2020 ¹⁷ | Serious | Low | Low | Low | Low | Moderate | Low | Serious |
| Potluri, 2020*.20 | Serious | No information | Low | Low | No information | No information | No information | Serious |
| Vincent, 2020 ⁷ | Moderate | Low | Low | Low | Low | Moderate | Low | Moderate |
| Witberg, 2020 ²¹ | Moderate | Low | Low | Low | No information | Moderate | Low | Moderate |
| Elbaz-Greener, 2017 ⁶ | Serious | Low | Low | Low | Low | Moderate | Low | Serious |
| | | Life-thr | eatening and maj | or access site bleed | ling complication | s | · | |
| Kotronias, 2020 ¹⁷ | Serious | Low | Low | Low | Low | Moderate | Low | Serious |
| Potluri, 2020*.20 | Serious | No information | Low | Low | No information | No information | No information | Serious |

| Vincent, 2020 ⁷ | Moderate | Low | Low | Low | Low | Moderate | Low | Moderate |
|----------------------------------|----------|----------------|-----------------|-------------------|----------------|----------------|----------------|----------|
| Witberg, 2020 ²¹ | Moderate | Low | Low | Low | No information | Moderate | Low | Moderate |
| Moriyama, 2019 ¹⁸ | Moderate | Low | Low | Low | No information | No information | No information | Moderate |
| Elbaz-Greener, 2017 ⁶ | Serious | Low | Low | Low | Low | Moderate | Low | Serious |
| | | <u> </u> | Minor access si | ite bleeding comp | lications | | | |
| Kotronias, 2020 ¹⁷ | Serious | Low | Low | Low | Low | Moderate | Low | Serious |
| Potluri, 2020*,20 | Serious | No information | Low | Low | No information | No information | No information | Serious |
| Vincent, 2020 ⁷ | Moderate | Low | Low | Low | Low | Moderate | Low | Moderate |
| Witberg, 2020 ²¹ | Moderate | Low | Low | Low | No information | Moderate | Low | Moderate |
| Elbaz-Greener, 2017 ⁶ | Serious | Low | Low | Low | Low | Moderate | Low | Serious |
| | | <u> </u> | Transfusi | on of red blood c | ells | | | |
| Vincent, 2020 ⁷ | Moderate | Low | Low | Low | Low | Moderate | Low | Moderate |
| Witberg, 2020 ²¹ | Moderate | Low | Low | Low | No information | Moderate | Low | Moderate |
| Elbaz-Greener, 2017 ⁶ | Serious | Low | Low | Low | Low | Moderate | Low | Serious |

*Since the study by Potluri and colleagues¹⁹ did not report sufficient data to ascertain access site-related bleeding complications, bleeding outcomes were taken from Basra and colleagues²⁰; a study from the same center and authors with an overlapping study time periods that provided sufficient data to adjudicate bleeding events as access site-related. Quality assessment was based on the information that was available in Basra and colleagues.

Table III. GRADE Assessment of overall strength of evidence

| Certainty assessment | | | | | № of patients | | F | ffect | | • | | |
|----------------------|--------------|-----------------|---------------|--------------|---------------|-------------------------|------------|-------------|----------------------|----------------------|-----------|------------|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Ultrasound | Fluoroscopy | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |

Major and minor access site vascular complications

| 7 | observational studies | very serious ^a | serious ^b | not serious ^e | not serious ^d | all plausible residual confounding would reduce the demonstrated effect | 220/2002 (11.0%) | 231/1560 (14.8%) | OR 0.54 (0.37 to 0.80) | 62 fewer per 1,000 (from 88 fewer to 26 fewer) | ⊕⊖⊖⊖ VERY LOW | CRITICAL |
|---|--------------------------|------------------------------|----------------------|--------------------------|--------------------------|---|---------------------|---------------------|-------------------------------|--|------------------|----------|
|---|--------------------------|------------------------------|----------------------|--------------------------|--------------------------|---|---------------------|---------------------|-------------------------------|--|------------------|----------|

Major access site vascular complications

| 8 | observational studies | very serious ^a | not serious ^e | not serious ^c | not serious ^d | all plausible residual confounding would | 98/2218 (4.4%) | 113/1646 (6.9%) | OR 0.51 (0.35 to 0.74) | 32 fewer per 1,000 (from 44 | ⊕○○○ VERY LOW | CRITICAL |
|---|--------------------------|------------------------------|--------------------------|--------------------------|--------------------------|--|----------------|--------------------|-------------------------------|---|------------------|----------|
| | | | | | | reduce the | | | | fewer to 17 | | |
| | | | | | | demonstrated effect | | | | fewer) | | |
| | | | | | | | | | | | | |

Minor access site vascular complications

| 7 | observational studies | very serious ^a | not serious ^e | not serious ^c | not serious ^d | all plausible residual confounding would reduce the demonstrated effect | 122/2150 (5.7%) | 122/1560 (7.8%) | OR 0.59 (0.38 to 0.91) | 31 fewer per 1,000 (from 47 fewer to 7 fewer) | ⊕○○○ VERY LOW | CRITICAL |
|---|--------------------------|------------------------------|--------------------------|--------------------------|--------------------------|---|--------------------|--------------------|-------------------------------|---|------------------|----------|
|---|--------------------------|------------------------------|--------------------------|--------------------------|--------------------------|---|--------------------|--------------------|-------------------------------|---|------------------|----------|

Life threatening, major and minor access site bleeding complications

| | Certainty assessment | | | | | | № of patients | | Effect | | Certainty | Importance |
|-----------------|--------------------------|------------------------------|----------------------|--------------------------|--------------------------|---|---------------------|---------------------|-------------------------------------|---|------------------|------------|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Ultrasound | Fluoroscopy | Relative (95% CI) | Absolute (95% CI) | Certainty | ттроглапсе |
| 5 | observational studies | very serious ^a | serious ^b | not serious ^e | not serious ^d | all plausible residual confounding would reduce the demonstrated effect | 143/1404 (10.2%) | 131/1086 (12.1%) | OR 0.59 (0.39 to 0.90) | 46 fewer per 1,000 (from 70 fewer to 11 more) | ⊕○○○ VERY LOW | CRITICAL |

Life-threatening and major access site bleeding complications

| 6 | observational studies | very serious ^a | serious ^b | not serious ^c | serious ^f | all plausible residual confounding would reduce the demonstrated effect | 75/1539 (4.9%) | 87/1221 (7.1%) | OR 0.52 (0.26 to 1.04) | 33 fewer per 1,000 (from 52 fewer to 3 more) | ⊕○○○ VERY LOW | CRITICAL |
|---|--------------------------|------------------------------|----------------------|--------------------------|----------------------|---|----------------|----------------|-------------------------------|--|------------------|----------|
| | | | | | | | | | | l I | | |

Minor access site bleeding complications

| reduce the fewer to 15 more) | 5 | observational studies | very seriousª | serious ^b | not serious ^c | serious ^f | all plausible residual confounding would reduce the demonstrated effect | 70/1404 (5.0%) | 56/1086 (5.2%) | OR 0.67 (0.34 to 1.31) | 16 fewer per 1,000 (from 33 fewer to 15 more) | ⊕○○○ VERY LOW | CRITICAL |
|------------------------------|---|--------------------------|------------------|----------------------|--------------------------|----------------------|---|----------------|----------------|-------------------------------|---|------------------|----------|
|------------------------------|---|--------------------------|------------------|----------------------|--------------------------|----------------------|---|----------------|----------------|-------------------------------|---|------------------|----------|

Transfusion of red blood cells

| | Certainty assessment | | | | | | № of patients | | Effect | | Certainty | Importance |
|-----------------|--------------------------|------------------------------|----------------------|--------------------------|----------------------|---|---------------|---------------|-------------------------------|--|------------------|------------|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Ultrasound | Fluoroscopy | Relative (95% CI) | Absolute (95% CI) | Certainty | ттроглапсе |
| 3 | observational studies | very serious ^a | serious ^e | not serious ^c | serious ^f | all plausible residual confounding would reduce the demonstrated effect | 78/902 (8.6%) | 68/846 (8.0%) | OR 0.73 (0.19 to 2.74) | 20 fewer per 1,000 (from 64 fewer to 113 more) | ⊕○○○ VERY LOW | IMPORTANT |

^a very serious risk of bias is due to the inclusion of studies of moderate to high risk of bias according to the Robins I tool. ^b: serious, moderate variation in point estimates with some overlap in CIs and substantial heterogeneity. ^c: unimportant as studies represent a selection of valve systems with varying prevalence of peripheral arterial disease. ^d: not serious as confidence intervals do not overlap with line of no effect with adequate total number of events. ^e: Unimportant, some variation in point estimates with large overlap in CIs and moderate heterogeneity. ^f: serious as confidence intervals overlap with line of no effect with generally small number of events. ^g:serious as confidence intervals overlap with line of no effect despite the adequate number of events. *CI: Confidence interval; OR: Odds ratio.*

Table IV. Outcomes according to imaging modality

| Study | Criteria | Outcomes | Ultrasound (events/total) | Fluoroscopy (events/total) | Adjusted odds ratio |
|-----------------------|----------|---|------------------------------|-------------------------------|------------------------------|
| | | | | | (95% confidence interval) |
| | | Major and minor access site VCs | 22/393 (5.6%) | 21/125 (16.8%) | 0.33 (0.11-0.94) |
| | | Major access site VCs | 12/393 (3.05%) | 7/125 (5.6%) | 0.53 (0.20-1.38) |
| Kotronias | VARC-2 | Minor access site VCs | 10/393 (2.54%) | 14/125 (11.2%) | 0.31 (0.11-0.85) |
| 202017 | | Life-threatening, major and minor access site BCs | 17/393 (4.33%) | 12/125 (9.6%) | - |
| | | Life-threatening and major access site BCs | 10/393 (2.54%) | 3/125 (2.4%) | - |
| | | Minor access site BCs | 7/393 (1.78%) | 9/125 (7.2%) | - |
| | | Major and minor access site VCs | 27/380 (7.9%) | 29/232 (14.2%) | - |
| | | Major access site VCs | 12/380 (3.2%) | 13/232 (5.6%) | - |
| Potluri | | Minor access site VCs | 15/380 (3.9%) | 16/232 (6.9%) | - |
| 2020 ^{19,20} | VARC-2 | Life-threatening, major and minor access site BCs* [†] | 5/109 (4.59%) | 9/115 (7.83%) | - |
| | | Major and life-threatening access site BCs [†] | 5/109 (4.59%) | 7/115 (6.09%) | - |
| | | Minor access site BCs [†] | 0/109 (0%) | 2/115 (1.74%) | - |
| | | Major and minor access site VCs | 13/95 (13.7%) | 28/95 (29.5%) | 0.37 (0.17-0.77) |
| | | Major access site VCs | 4/95 (4.2%) | 12/95 (12.6%) | 0.31 (0.12-0.85) |
| Vincent | VARC-2 | Minor access site VCs | 9/95 (9.5%) | 16/95 (16.8%) | 0.61 (0.24-1.52) |
| 20207 | | Life-threatening, major and minor access site BCs | 13/95 (13.7%) | 26/95 (27.4%) | 0.42 (0.20-0.88) |
| | | Life-threatening and major access site BCs | 4/95 (4.2%) | 12/95 (12.6%) | 0.30 (0.09-0.96) |
| | | Minor access site BCs | 9/95 (9.5%) | 14/95 (14.7%) | 0.61 (0.25-1.48) |
| | | Transfusion of RBCs | 11/95 (11.6%) | 20/95 (21.1%) | 0.48 (0.21-1.09) |
| | | Major and minor access site VCs | 36/529 (6.8%) | 43/642 (6.7%) | 1.12 (0.65-1.96) |
| | | Major access site VCs | 16/529 (3.0%) | 16/642 (2.6%) | 1.14 (0.51-2.78) |
| | | Minor access site VCs | 20/529 (3.8%) | 27/642 (4.0%) | 0.89 (0.39-2.04) |
| Witherg | | Life-threatening, major and minor access site BCs | 34/529 (6.4%) | 38/642 (5.9%) | 1.06 (0.61-1.92) |
| 2020 ²¹ | VARC-2 | Life-threatening and major access site BCs* | 19/529 (3.6%) | 18/642 (2.8%) | - |
| | | Life-threatening access site BCs | 8/529 (1.5%) | 11/642 (1.7%) | 0.83 (0.59-3.13) |
| | | Major access site BCs | 11/529 (2.1%) | 7/642 (1.1%) | 1.35 (0.40-3.23) |
| | | Minor access site BCs | 15/529 (2.8%) | 20/642 (3.1%) | 0.80 (0.58-3.45) |
| | | Transfusion of RBCs | 44/529 (8.3%) | 24/642 (3.7%) | 2.85 (1.32-5.88) |

| Bouteau | | Major and minor access site VCs* | 61/340 (17.9%) | 51/222 (23.0%) | - |
|-------------------|--------|--|----------------|----------------|------------------|
| 201914,15 | - | Major access site VCs | 19/340 (5.6%) | 23/222 (10.4%) | - |
| | | Minor access site VCs | 42/340 (12.4%) | 28/222 (12.6%) | - |
| | | Major and minor access site VCs* | 5/135 (3.7%) | 21/135 (15.6 | 0.21 (0.08-0.57) |
| Moriyama | - | Major access site VCs | 2/135 (1.5%) | 10/135 (7.4%) | 0.19 (0.04-0.87) |
| 201918 | | Minor access site VCs | 3/135 (2.2%) | 11/135 (8.2%) | 0.26 (0.07-0.94) |
| | | Life-threatening and major access site BCs | 2/135 (1.5%) | 12/135 (8.9%) | 0.15 (0.03-0.70) |
| Khan | VARC-2 | Major access site VCs | 0/68 (0%) | 4/86 (4.65%) | - |
| 201916 | | | | | |
| | | Major and minor access site VCs* | 56/278 (20.2%) | 38/109 (34.9%) | - |
| | | Major access site VCs | 33/278 (11.9%) | 28/109 (25.7%) | - |
| | | Minor access site VCs | 23/278 (8.3%) | 10/109 (9.2%) | - |
| Elbaz- Greener | VARC-2 | Life-threatening, major and minor access site BCs* | 74/278 (26.6%) | 46/109 (42.2%) | - |
| 20176 | | Major and life-threatening access site BCs | 35/278 (12.6%) | 35/109 (32.1%) | - |
| | | Major access site BCs | 30/278 (10.8%) | 28/109 (25.7%) | - |
| | | Minor access site BCs | 39/278 (14.0%) | 11/109 (10.1%) | - |
| | | Transfusion of RBCs | 23/278 (8.3%) | 24/109 (22.0%) | - |

*: calculated from already known data assuming life-threatening, major and minor categories are assumed as separate entities, as per VARC criteria. [†]: Since the study by Potluri and colleagues¹⁹ did not report sufficient data to ascertain access site related bleeding complications, bleeding outcomes were taken from Basra and colleagues²⁰; a study from the same center and authors with a overlapping study time periods that provided sufficient data to adjudicate bleeding events as access site related; *BCs: Bleeding complications; RBCs: red blood cells; VARC-2: Valve Academic Research Consortium-2; VCs: vascular complications.*

Sensitivity **Outcomes** analysis Aspect interrogated OR (95% CI) domain Total access site vascular complications 0.44 (0.20-0.99) Major access site vascular complications 0.49 (0.24-1.02) Minor access site vascular complications 0.51 (0.29-0.90) Maximally Total access site bleeding complications 0.69 (0.28-1.70) adjusted outcomes Life-threatening and major access site 0.23 (0.09-0.60) bleeding complications Minor access site bleeding complications 0.70 (0.37-1.31) Transfusion of red blood cells 0.66 (0.13-3.27) Data analysed Total access site vascular complications 0.42 (0.20-0.89) Major access site vascular complications 0.51 (0.23-1.16) Minor access site vascular complications 0.43 (0.20-0.90) 'Moderate' Total access site bleeding complications 0.71 (0.28-1.80) Risk of Bias only Life-threatening and major access site 0.44 (0.12-1.71) bleeding complications Minor access site bleeding complications 0.78 (0.46-1.34) Transfusion of red blood cells 1.47 (0.97-2.22) Inverse variance No change Total access site vascular complications 0.56 (0.46-0.69) Major access site vascular complications 0.51 (0.38-0.68) 0.66 (0.51-0.86) Minor access site vascular complications Analysis Fixed effect Total access site bleeding complications 0.63 (0.48-0.82) methods meta-analysis Life-threatening and major access site 0.52 (0.37-0.72) bleeding complications Minor access site bleeding complications 0.79 (0.54-1.15) Transfusion of red blood cells 0.94 (0.67-1.32) Total access site vascular complications 0.45 (0.32-0.63) I²: 47% Sequential Heterogeneity removal 0.75 (0.55-1.02) I²: 12% Minor access site vascular complications algorithm to

Table V. Sensitivity Analyses

| reach I ² <50% | Total access site bleeding complications | 0.47 (0.34-0.66) I ² : 0% |
|---------------------------|---|---------------------------------------|
| | Life-threatening and major access site bleeding complications | 0.39 (0.22-0.68) I ² : 30% |
| | Minor access site bleeding complications | 0.94 (0.59-1.49) I ² : 10% |

Moderate Risk of Bias shows outcomes following the removal of studies at 'Serious' Risk of Bias. 'Total': major and minor vascular complications/ life-threatening, major and minor bleeding complications. *CI: confidence interval; I²: heterogeneity; OR: odds ratio*

| Table V | I. Table | indicating | methods | of adjustme | ent and co | ovariates | of adjustment. |
|---------|----------|------------|---------|-------------|------------|-----------|----------------|
| | | | | | | | |

| Study | Outcome | Method | Adjustment covariates |
|------------------------------|--|----------------------------------|--|
| Kotronias 2020 ¹⁸ | Vascular complications | Multivariate logistic regression | Year of operation, LV-guidewire pacing, peripheral arterial disease |
| Vincent 2020 ⁷ | Vascular and bleeding complications | Propensity matching | Age, gender, BMI, NYHA class III or IV, STS-PROM Score, Anticoagulant, Diabetes, Hypertension, Coronary artery disease, prior cerebrovascular disease, chronic obstructive airways disease, peripheral arterial disease; prior atrial fibrillation,, renal function, LVEF, aortic valve area, mean aortic gradient, primary access sheath size, secondary access sheath size, prosthesis size, sheath to femoral artery ratio |
| Witberg 2020 ²¹ | Vascular and bleeding complications | Multivariate logistic regression | Age, sex, diabetes mellitus, glomerular filtration rate, previous stroke or transient ischaemic attack, peripheral vascular disease, body mass index, frailty, and general anaesthesia |
| Moriyama 2019 ¹⁸ | Vascular complications | Propensity matching | No information available |

BMI: Body mass index; LV: left ventricle; LVEF: left ventricle ejection fraction; NYHA: New York Heart Association; STS-PROM: Society of Thoracic Surgeons 30-Day Predicted Risk of Mortality.

Supplemental Figure

Figure I



Figure I: Meta-analyses evaluating maximally adjusted risk of life-threatening, major and minor access site bleeding complications (**S1A**), life-threatening and major access site bleeding complications (**S1B**) and minor access site bleeding complications (**S1C**) of an ultrasound-guided versus fluoroscopy-guided TAVR access strategy.