MÉDECINE SORBONNE UNIVERSITÉ

Action cœur

# Anti-thrombotic treatment after TAVR: insights from the FRANCE-TAVI Registry


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# Declaration of interest

- Research contracts (BMS/PFIZER)
- Others (Honorarium as a speaker for Bayer, Astra-Zeneca and BMS)

# Management of antithrombotics in patients with TAVI

| Bioprosthesis | Class | Level |
|---|---|---|
| **Anticoagulation** | | |
| DAPT should be considered for the first 3–6 months after TAVI, followed by lifelong SAPT in patients who do not need OAC for other reasons. | IIa | C |

# Management of antithrombotics in patients with TAVI

| Bioprosthesis | Class | Level |
|---|---|---|
| **Anticoagulation** | | |
| SAPT may be considered after TAVI in the case of high bleeding risk. | IIb | C |
| OAC may be considered for the first 3 months after surgical implantation of an aortic bioprosthesis. | IIb | C |

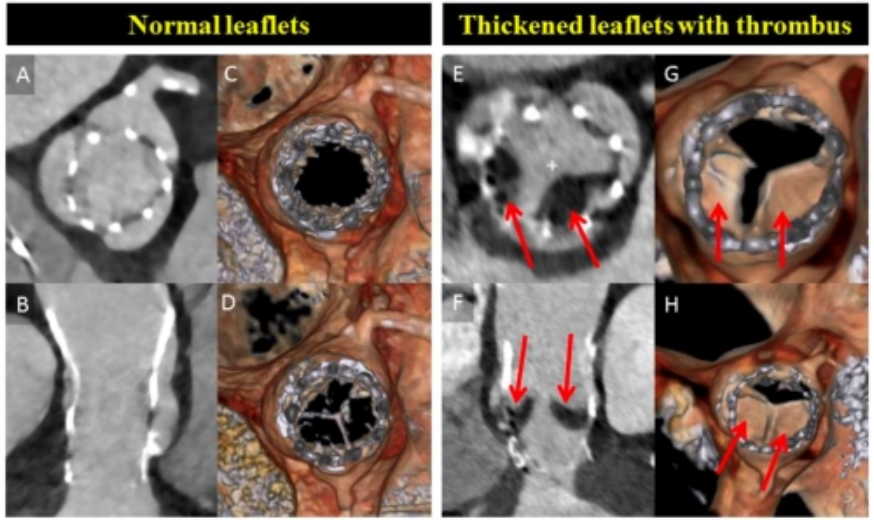
# DETERMINANTS OF ANTITHROMBOTIC TX?

- 1/3→ SCAD or stent PCI
- 1/3 → Secondary prevention for stroke
- 2/5 → Permanent AF or NOAF

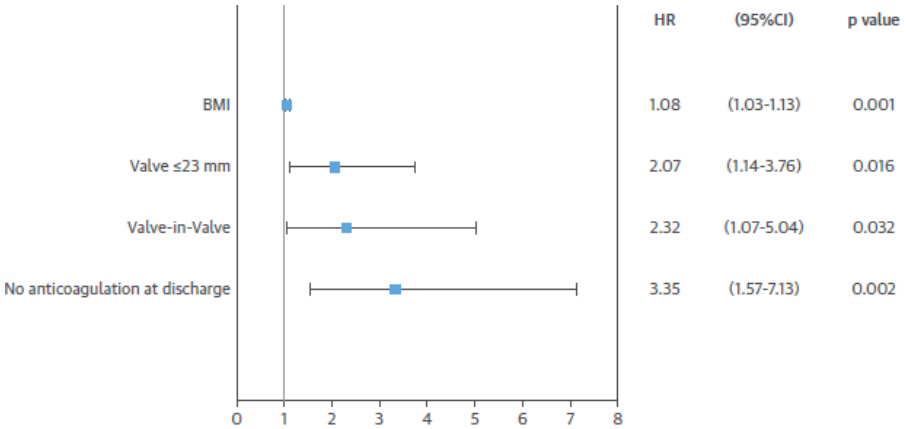
- 30%→ Antiplatelet Therapy alone
- 50% → Oral Anticoagulation alone
- 25% → OAC + APT

# BIOPROSTHETIC VALVE DYSFUNCTION

- ↗ in mean gradient (MG) ≥ 10 mmHg or new MG ≥ 20mmHg
- Prevalence of 4.5% post-TAVR




Makkar et al, NEJM, 2015




*Del trigo et al, JACC, 2016*

# OBJECTIVES

- To investigate whether **anti-thrombotic treatment** influences **long-term mortality and early bioprosthetic valve dysfunction*** (↗ prosthetic gradient ≥10 mmHg or new gradient≥20 mmHg)

- To explore **independent correlates** of long-term mortality and early BVD after TAVI.

*Eur. Heart J. 2017;38:3382–3390

# STUDY OVERSIGHT

- **Nation-wide France-Tavi Registry***
- **Sponsors→** Société Française de Cardiologie
- **Fundings →** Edwards Life Science, Medtronic, Action-Coeur
- **Statistical Analysis →** StatEthic and Action-Coeur

*Auffret, V. et al. J Am Coll Cardiol. 2017;70(1):42–55.

# METHODS

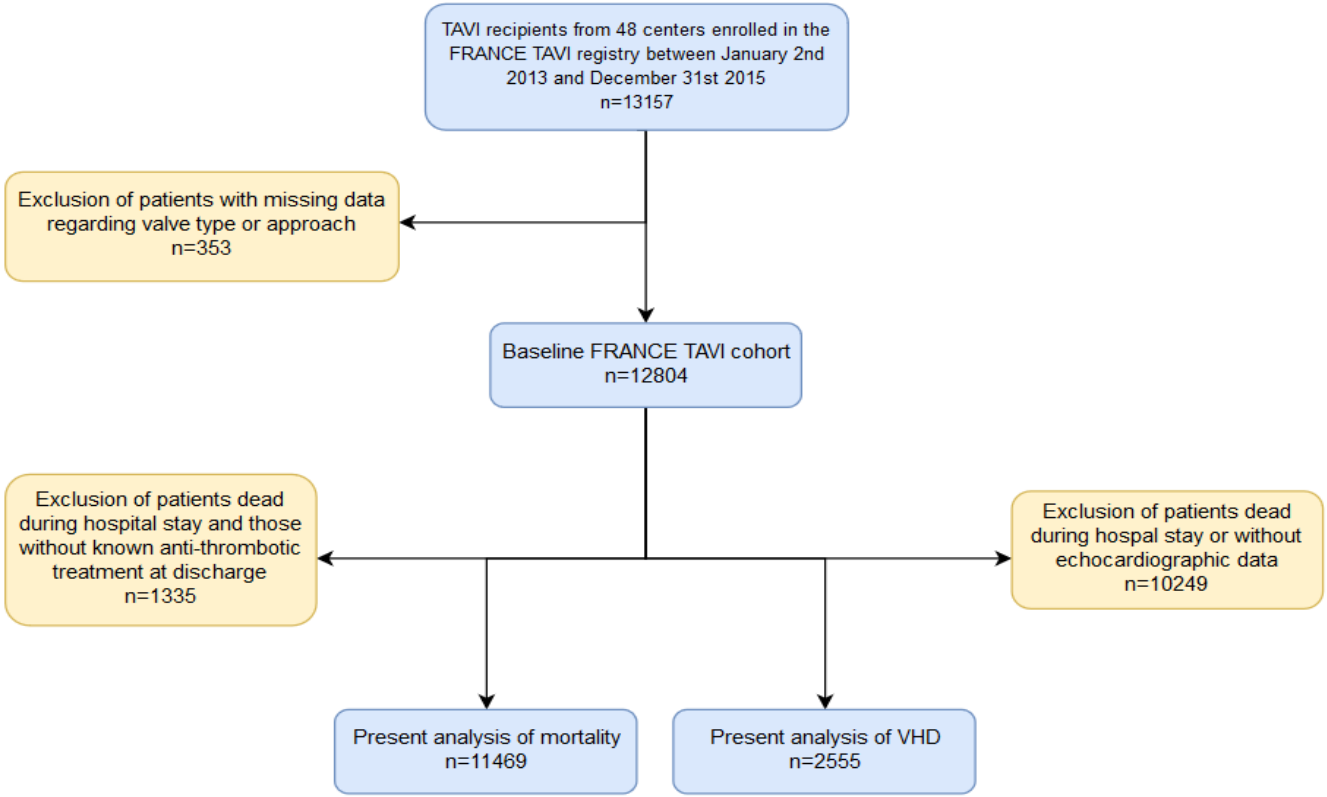
## Database: FRANCE TAVI

- **Inclusion** → multi-centre, French, prospective, registry
- **Period** → January 2013 and December 2015
- **Mortality outcome** → INSEE query on April 12th 2016
- **BVD** → Echocardiographic follow-up to May 9th, 2016

## Statistical analysis

- **Missing values** → multiple imputation (sensitivity analysis and complete cases)
- **Multivariable Cox regression** for mortality
- **Multivariable logistic regression** for Bioprosthetic Valve Dysfunction
- IBM SPSS Version 23.0 (Armonk, NY: IBM Corp) software

# FLOW CHART


TAVI recipients from 48 centers enrolled in the FRANCE TAVI registry between January 2nd 2013 and December 31st 2015
n=13157
Exclusion of patients with missing data regarding valve type or approach
n=353
Baseline FRANCE TAVI cohort
n=12804
Exclusion of patients dead during hospital stay and those without known anti-thrombotic treatment at discharge
n=1335
Exclusion of patients dead during hospal stay or without echocardiographic data
n=10249
Present analysis of mortality
n=11469
Present analysis of VHD
n=2555

# PATIENTS CHARACTERISTICS

| Characteristics * | Total (n=11469) | No OAC (n=7633) | OAC (n=3836) | P value |
|---|---|---|---|---|
| **Age** | 82.8 (0.068) | 82.7 (0.085) | 82.9 (0.111) | 0.6 |
| **BMI (kg/m²)** | 26.7 (0.056) | 26.6 (0.070) | 26.9 (0.094) | <0.001 |
| **Gender (male)** | 5683 (49.6) | 3712 (48.6) | 1971 (51.4) | 0.005 |
| **NYHA class III-IV** | 7941 (68.9) | 5214 (68.2) | 2727 (71) | 0.002 |
| **Logistic Euroscore I** | 17.8 (0.114) | 17.3 (0.139) | 18.9 (0.198) | <0.001 |
| **Prior CABG** | 1327 (11.6) | 906 (11.9) | 421 (11) | 0.34 |
| **Prior TAVR** | 114 (1.0) | 71 (0.9) | 43 (1.1) | 0.17 |
| **Prior non-CABG surgery** | 798 (6.9) | 457 (6.0) | 341 (8.9) | <0.001 |

* Data are number (%) or mean+-standard error

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# PATIENTS CHARACTERISTICS

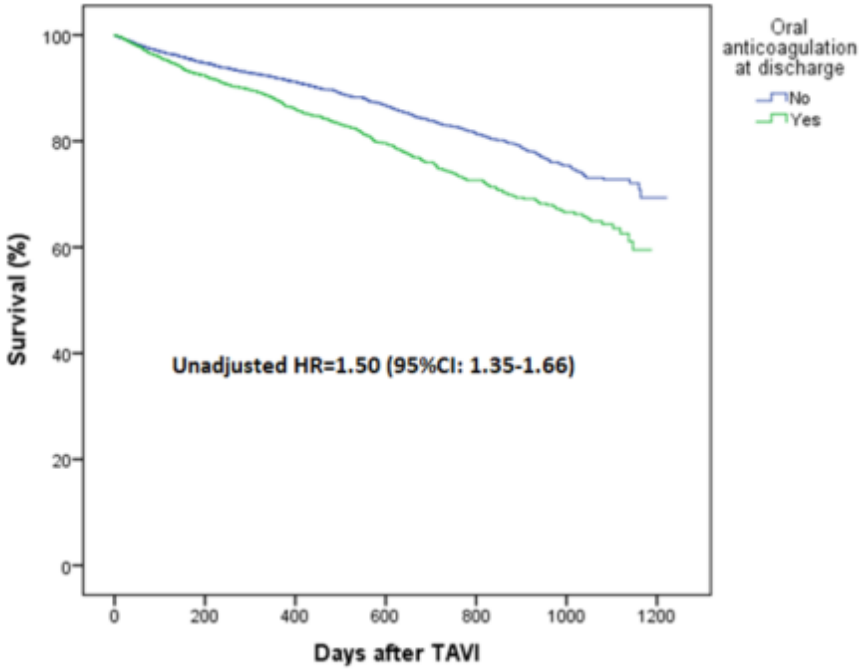
| Characteristics | Total (n=11469) | No OAC (n=7633) | OAC (n=3836) | |
|---|---|---|---|---|
| Chronic renal failure (eGFR<60mL/min) | 5069 (44.2) | 3232 (42.3) | 1837 (47.9) | <0.001 |
| Atrial fibrillation | 3789 (33.0) | 1066 (14.0) | 2723 (70.8) | <0.001 |
| LVEF (%) | 55.4 (0.128) | 56.1 (0.150) | 53.8 (0.217) | <0.001 |
| Non-femoral access | 1895 (16.5) | 1194 (15.6) | 701 (18.3) | <0.001 |
| Self-expandable (vs balloon) valve | 4045 (35.3) | 2714 (35.6) | 1331 (34.7) | 0.37 |
| Prosthesis diameter ≤23 mm | 3215 (28.2) | 2258 (29.6) | 957 (24.9) | <0.001 |
| AR moderate to severe post-TAVR | 1151 (10.0) | 758 (10) | 393 (10.3) | 0.6 |
| Aspirin at discharge | 9554 (83.3) | 7123 (93.3) | 2431 (63.4) | <0.001 |
| Dual therapy | 2100 (18.3) | 0 | 2100 (54.7) | <0.001 |
| Triple Therapy | 331 (2.9) | 0 | 331 (8.6) | <0.001 |

* Data are number (%) or mean+-standard error

# Correlates of Long-Term Mortality

| N=11469 | MI p-value | Adj. HR | 95%CI lower | 95%CI upper |
|---|---|---|---|---|
| Gender (male) | <0.001 | 1.63 | 1.44 | 1.84 |
| NYHA III or IV | <0.001 | 1.28 | 1.14 | 1.46 |
| Euroscore I | <0.001 | 1.01 | 1.01 | 1.02 |
| Prior CABG | <0.001 | 0.64 | 0.54 | 0.77 |
| Prior non-CABG cardiac surgery | <0.001 | 0.59 | 0.46 | 0.76 |
| Diabetes | <0.001 | 1.25 | 1.12 | 1.41 |
| Moderate/severe renal failure | <0.001 | 1.37 | 1.23 | 1.53 |
| Atrial fibrillation | <0.001 | 1.41 | 1.23 | 1.62 |
| Non-femoral access for TAVR | 0.011 | 1.18 | 1.04 | 1.35 |
| Moderate to severe prosthetic regurgitation | 0.001 | 1.28 | 1.11 | 1.50 |
| Anticoagulation at discharge | 0.013 | 1.18 | 1.04 | 1.35 |
| Auto-expandable (vs balloon) valve | 0.014 | 1.15 | 1.03 | 1.29 |
| Prosthesis diameter 23 mm or less | 0.042 | 1.17 | 1.01 | 1.36 |

# KM Curves According to Anticoagulation




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| No | | | | | | | |
| OAC | 7632 | 5282 | 3393 | 2123 | 1154 | 472 | 1 |
| OAC | 3835 | 2641 | 1635 | 1003 | 519 | 223 | 0 |

# Correlates of Bioprosthetic Valve Dysfunction

| N=2555 | m=20<br>P-value | Adj. OR | 95% CI<br>upper | 95% CI lower |
|---|---|---|---|---|
| **BMI** | 0.002 | 1.05 | 1.02 | 1.09 |
| **Prior TAVR** | 0.025 | 2.96 | 1.15 | 7.64 |
| **Moderate/severe renal failure** | 0.034 | 1.46 | 1.03 | 2.08 |
| **Non-femoral access** | 0.049 | 0.53 | 0.28 | 1.02 |
| **Prosthesis ≤23 mm** | <0.001 | 3.43 | 2.41 | 4.89 |
| **OAC at discharge** | 0.005 | 0.54 | 0.35 | 0.82 |

# DISCUSSION

- Post-TAVI ATT → Driven by patients characteristics
- OAC → Less BVD → Potential clinical benefit?
- OAC use → Colinear with the indication for AF → Mortality?

**70% patients were on OAC due to AF**

# LIMITATIONS

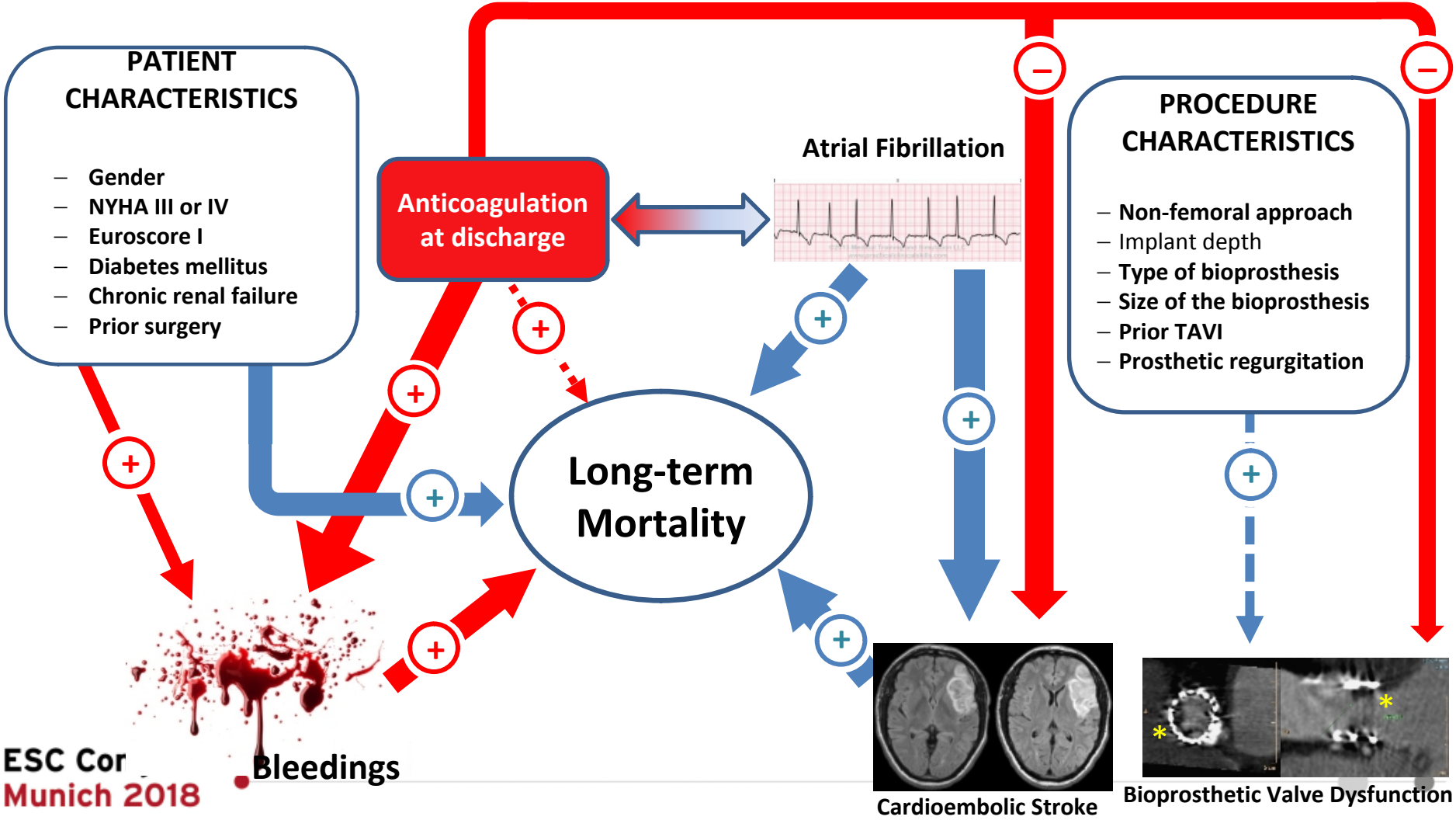
- Not randomized → unknown confounders
- Declarative clinical outcome reporting
- Treatment Cross-over → An issue in this elderly population
- Identification of BVD* with MSCT** →Different predictors?



* Bioprosthetic Valve Dysfuntion **Multislice Computed Tomography

# MAJOR ONGOING TRIALS

| | Treatment comparison | Number of patients | NVAF | Status |
|---|---|---|---|---|
| GALILEO | RIVA vs DAPT/SAPT | 1520 | Excluded | Enrolment completed |
| ATLANTIS | VKA vs Apixaban<br>DAPT/SAPT vs Apixaban | 1510 | Included (stratified) | Enrolment almost done |
| ENVISAGE | EDOXABAN | 1400 | only | Ongoing |
| POPULAR | VKA vs VKA+clopi<br>DAPT vs ASA | 1510 | Included and stratified | Ongoing |
| AVATAR | VKA vs VKA+APT | 170 | Included (stratified) | Ongoing |
| AUREA | VKA vs DAPT | 124 | Excluded | Ongoing |



Accepted in JACC

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY


# Long-Term Mortality and Early Valve Dysfunction According to Anticoagulation Use: The FRANCE-TAVI registry

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**ABSTRACT**

**BACKGROUND** The optimal anti-thrombotic treatment after transcatheter aortic valve replacement (TAVR) remains a matter of debate. Dual antiplatelet therapy (DAPT) is recommended but single antiplatelet therapy or oral anticoagulation (OAC) are frequently used according to the patient profile. Whether this may impact clinical outcome is unknown.

**METHOD** and objectives: FRANCE-TAVI is a prospective multicenter nation-wide French registry. Our objectives were to identify independent correlates of long-term all-cause mortality and early bioprosthetic valve dysfunction (BVD, defined as increased prosthetic gradient ≥10 mmHg or new gradient ≥20 mmHg).

**RESULTS** Of 12,804 patients included between January 1, 2013 and December 31, 2015, 11,469 (age 82.8±0.07 years old [mean±SE], logistic Euroscore 17.8±0.1%, mean duration follow-up was 495±3.5 days) were alive at discharge with known antithrombotic treatment and were analyzed for mortality. 2555 had at least 2 echocardiographic evaluations and were eligible of BVD assessment. One third of patients had a history of atrial fibrillation and the same proportion had OAC at discharge (n=3836). Neither aspirin nor clopidogrel were independently associated with mortality. Male gender (adj HR 1.63 [1.44-1.84], p<0.001), history of atrial fibrillation (adj. HR 1.41 [1.23-1.62], p<0.001) and chronic renal failure (adj. HR 1.37 [1.23-1.53], p<0.001) were the strongest independent correlates of mortality. Anticoagulation at discharge (adj. OR 0.54 [0.35-0.82], p=0.005) and a non-femoral approach (adj. OR 0.53 [0.28-1.02], p=0.049) were independently associated with lower rates of BVD, while chronic renal failure (adj. OR 1.46 [1.03-2.08], p=0.034) and prosthesis size ≤23mm (adj. OR 3.43 [2.41-4.89], p<0.001) yielded higher risk of BVD.

**CONCLUSIONS** Gender, renal failure and atrial fibrillation, impacted the most mortality at 3-year follow-up. In contrast anticoagulation (mostly given for atrial fibrillation) decreased the risk of BVD after TAVR. (J Am Coll Cardiol 2018;1:1)


**The presentation can be downloaded at action-cœur.org**