# Predicting paravalvular regurgitation after TAVI

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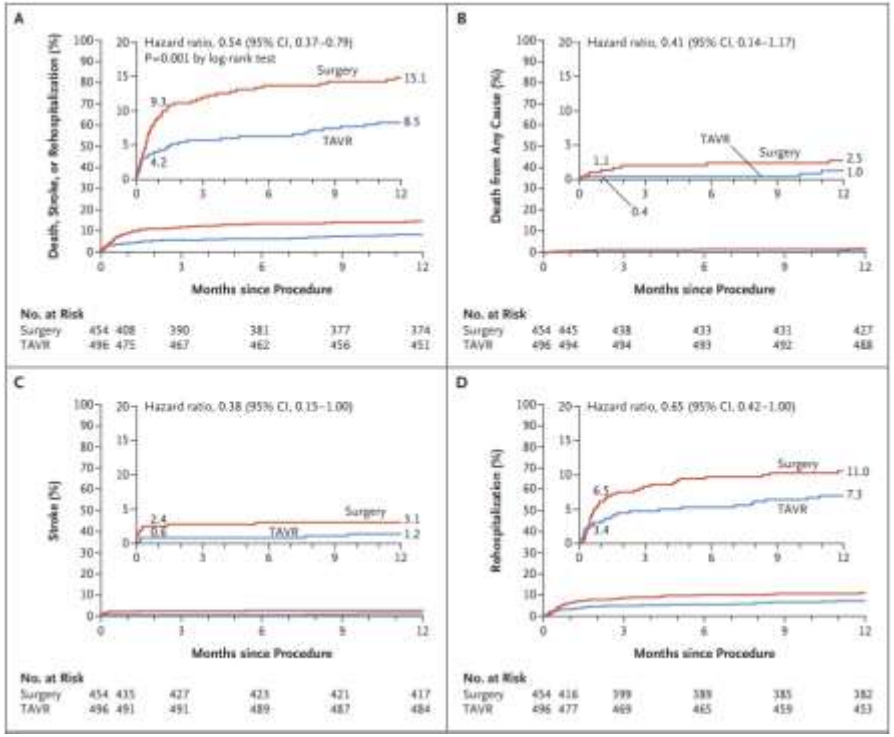
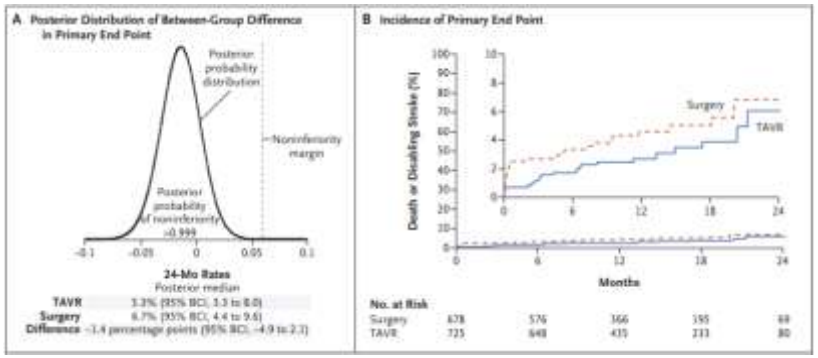
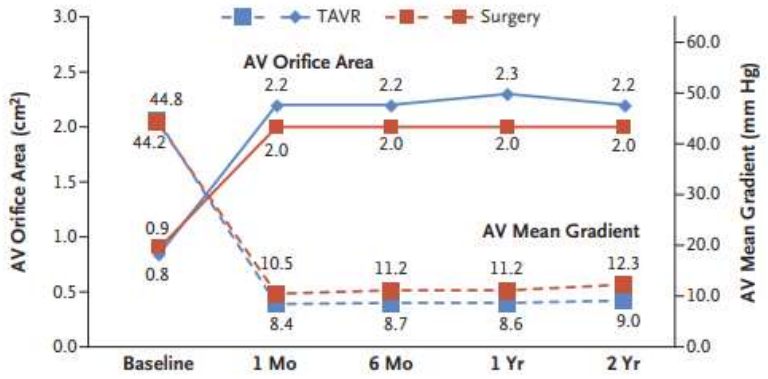
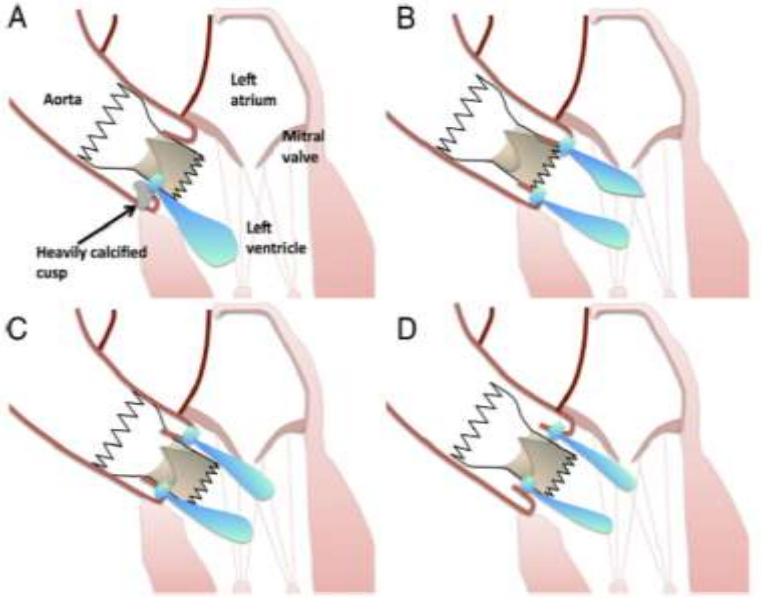
# Background

- Transcatheter aortic valve implantation (***TAVI***) is the new standard treatment of severe AS.
- Recent trials report that TAVI is ***superior/non-inferior*** to surgery in low surgical risk patients.
- However, ***paravalvular leakage*** (PVL) remains as one of the main limitations of TAVI procedure




Popma et al. N Engl J Med. 2019;380:1706, Reardon et al. N Engl J Med. 2017;376:1321, Sinning et al JACC 2012;59:1134

# Background

- PVL is associated with ***increased mortality***. Directly or indirectly? Still unknown.
- Factors associated with PVL
  - **Anatomical, clinical risk factors**
    - AV, aortic annulus calcification, anatomy of the aortic annulus, LVOT-ascending aorta angle
  - **Valvular, Procedural factors**
    - Generation of valve, size of valves, depth of implantation, pre/post balloon angioplasty, etc.

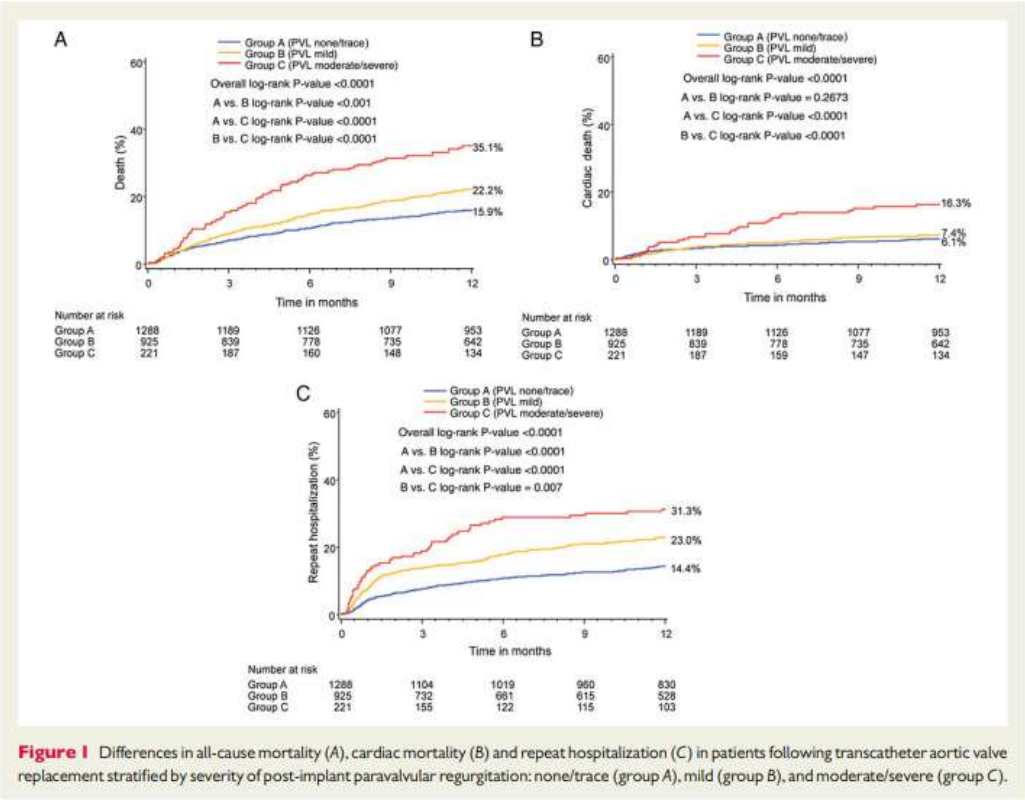
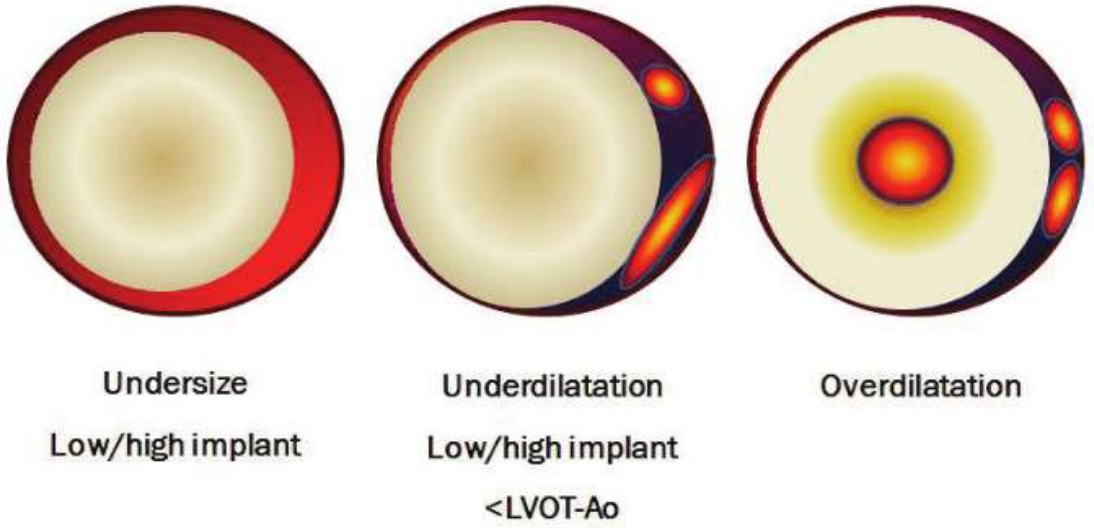



**Figure 1** Differences in all-cause mortality (*A*), cardiac mortality (*B*) and repeat hospitalization (*C*) in patients following transcatheter aortic valve replacement stratified by severity of post-implant paravalvular regurgitation: none/trace (group *A*), mild (group *B*), and moderate/severe (group *C*).



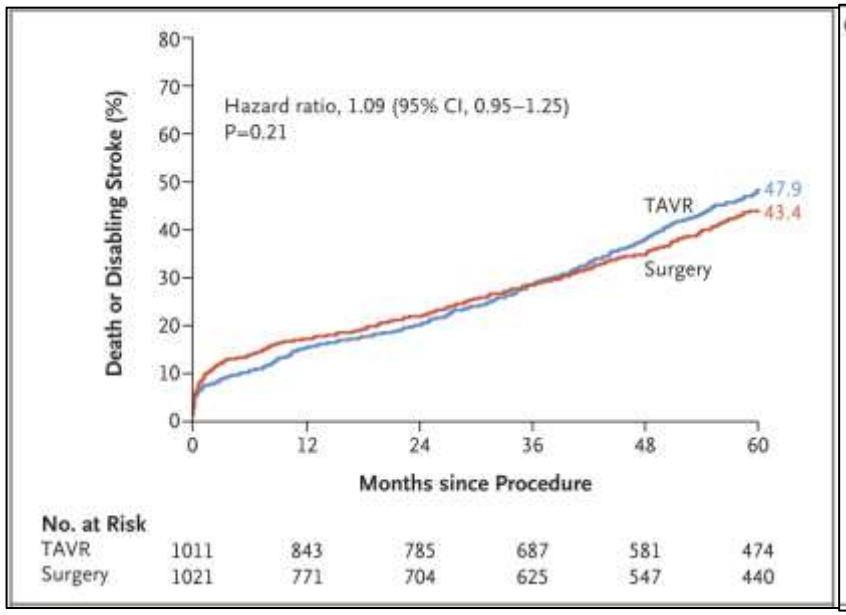
# Background

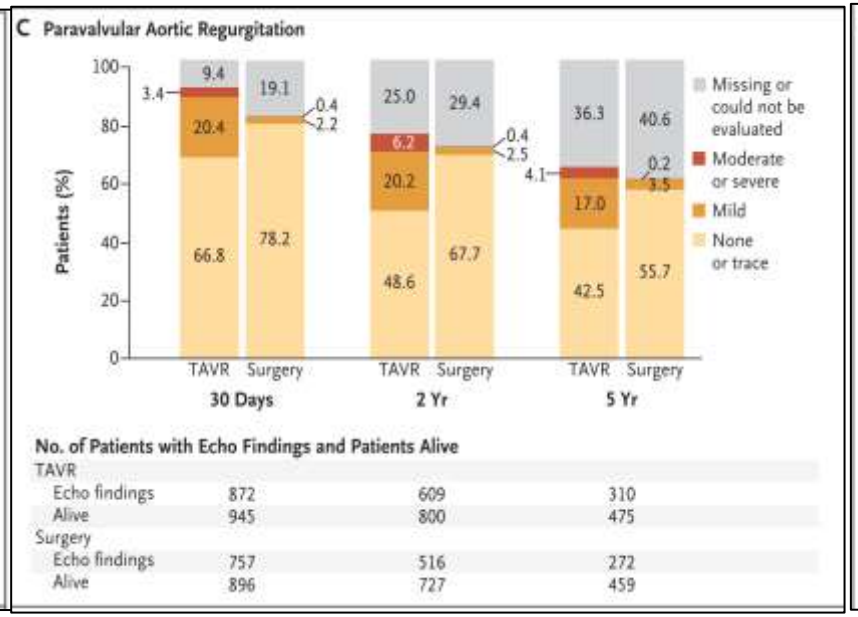
The NEW ENGLAND JOURNAL of MEDICINE
FEBRUARY 27, 2020

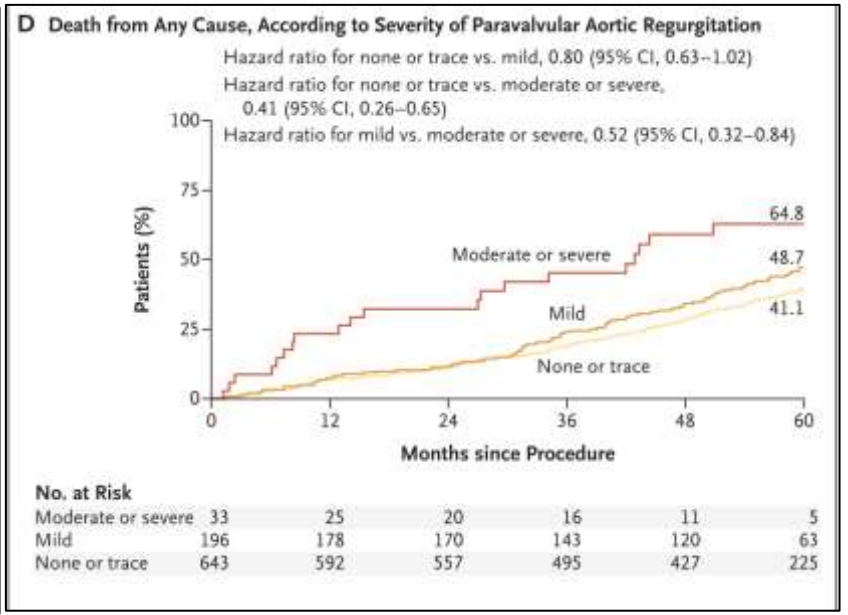
Five-Year Outcomes of Transcatheter or Surgical Aortic-Valve Replacement

R.R. Makkar, V.H. Thourani, M.J. Mack, S.K. Kodali, S. Kapadia, J.G. Webb, S.-H. Yoon, A. Trento, L.G. Svensson, H.C. Herrmann, W.Y. Szeto, D.C. Miller, L. Satler, D.J. Cohen, T.M. Dewey, V. Babaliaros, M.R. Williams, D.J. Kereiakes, A. Zajarias, R.L. Greason, B.K. Whisenant, R.W. Hodson, D.L. Brown, W.F. Fearon, M.J. Russo, P. Pibarot, R.T. Hahn, W.A. Jaber, E. Rogers, K. Xu, J. Wheeler, M.C. Alu, C.R. Smith, and M.B. Leon, for the PARTNER 3 Investigators*

- PVL may be MORE important in ***long-term***



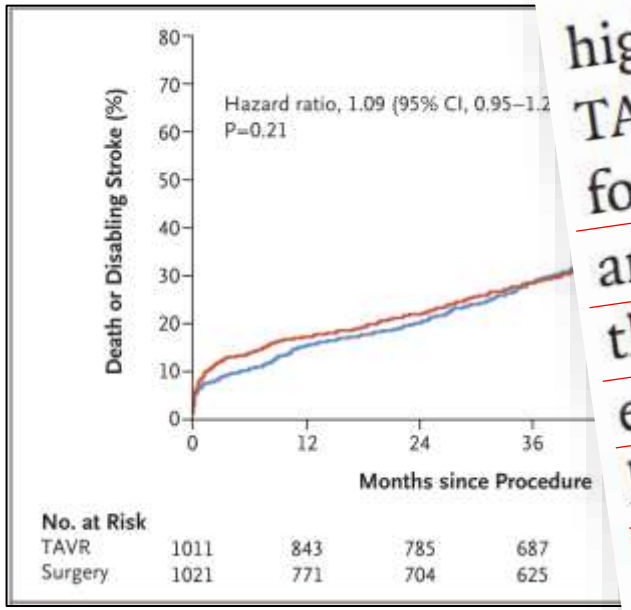



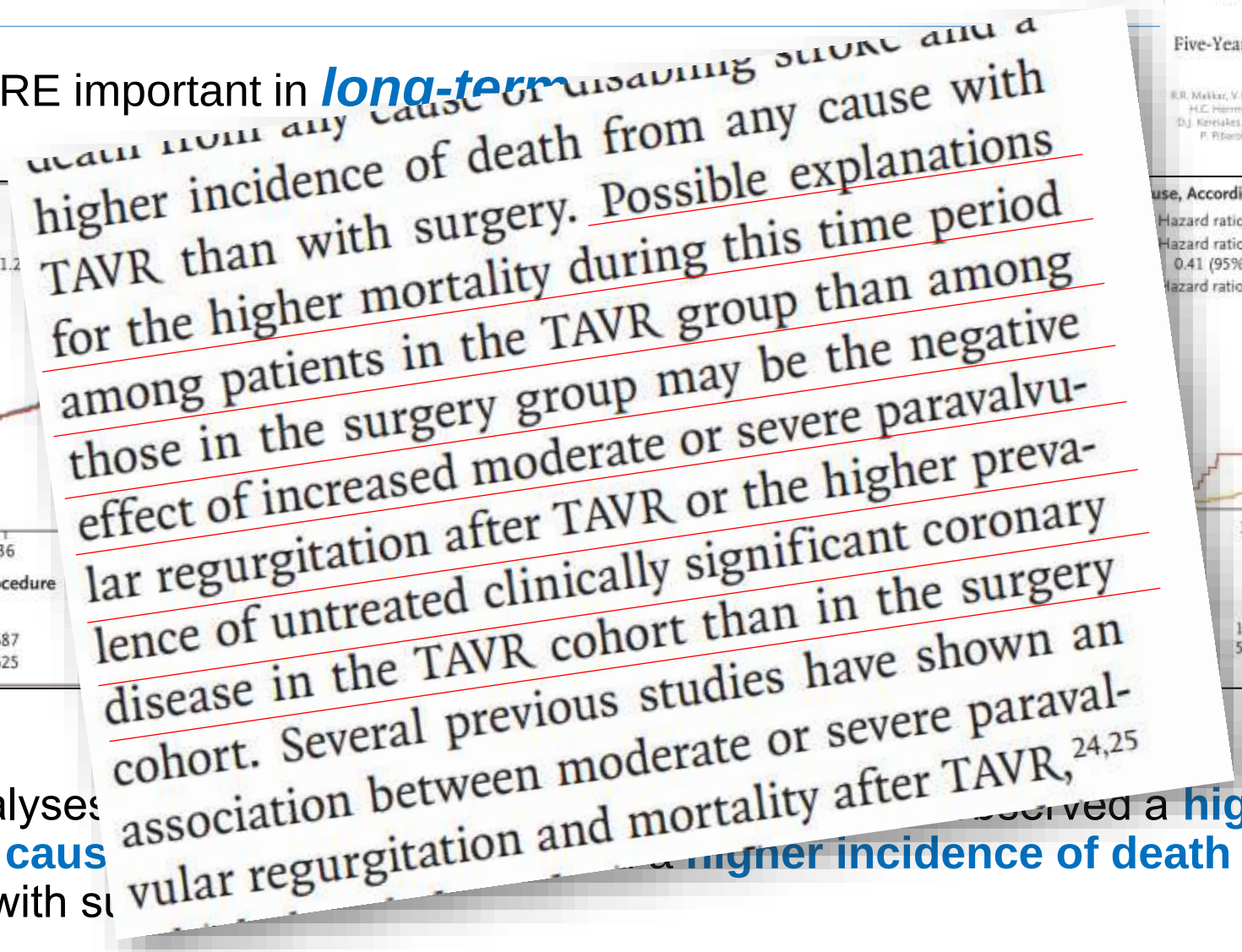

- "In landmark analyses from 2 to 5 years after the procedure, we observed a **higher incidence of death from any cause or disabling stroke** and a **higher incidence of death** from any cause with TAVR than with surgery"

Makkar, R.R., et al., N Engl J Med, 2020.

# Background

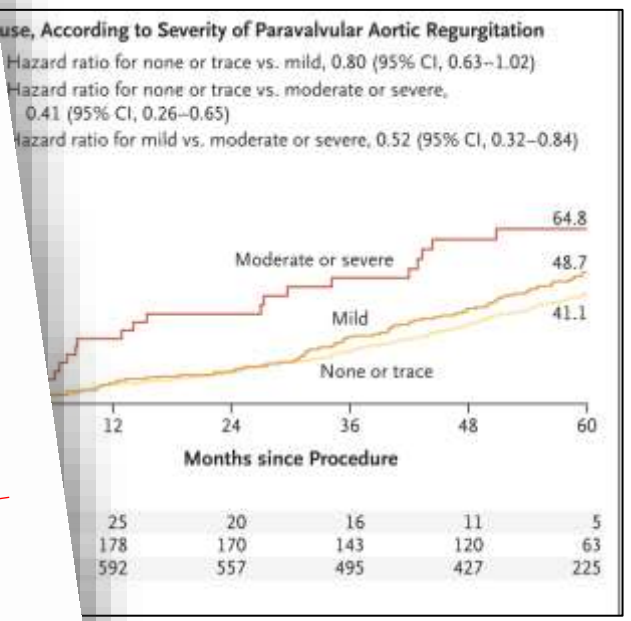
- PVL may be MORE important in ***long-term***





higher incidence of death from any cause with TAVR than with surgery. Possible explanations for the higher mortality during this time period among patients in the TAVR group than among those in the surgery group may be the negative effect of increased moderate or severe paravalvular regurgitation after TAVR or the higher prevalence of untreated clinically significant coronary disease in the TAVR cohort than in the surgery cohort. Several previous studies have shown an association between moderate or severe paravalvular regurgitation and mortality after TAVR,[24,25]


The NEW ENGLAND JOURNAL of MEDICINE
FEBRUARY 27, 2020

Five-Year Outcomes of Transcatheter or Surgical Aortic-Valve Replacement


Hazard ratio for none or trace vs. mild, 0.80 (95% CI, 0.63–1.02)
Hazard ratio for none or trace vs. moderate or severe, 0.41 (95% CI, 0.26–0.65)
Hazard ratio for mild vs. moderate or severe, 0.52 (95% CI, 0.32–0.84)
64.8
48.7
41.1
Moderate or severe
Mild
None or trace
Months since Procedure
25 20 16 11 5
178 170 143 120 63
592 557 495 427 225

- "In landmark analyses … observed a **higher incidence of death from any cause** with TAVR than with surgery

Makkar, R.R., et al., N Engl J Med, 2020.

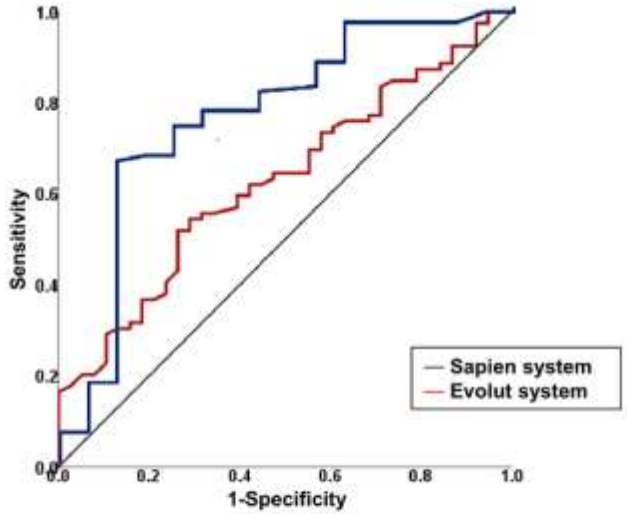
# How can we reduce (prevent) PVL ?

#1. Adequate Valve selection and sizing

#2. Precise evaluation and management

# Predictors of PVL

| | Univariable Analysis | | Multivariable Analysis | |
|---|---|---|---|---|
| **Total population** | **OR (95% CI)** | **P value** | **OR (95% CI)** | **P value** |
| **Leakage (-) proof valve** | **2.24 (1.21–4.13)** | **0.010*** | **3.19 (1.62–6.30)** | **0.001*** |
| **OI per a decrease by 5%** | **1.31 (1.05–1.62)** | **0.015*** | **1.45 (1.15–1.83)** | **0.001*** |
| **Total calcium amount >800** | **1.39 (0.72–2.70)** | **0.328** | | |
| **Calcium difference >200** | **1.23 (0.67–2.28)** | **0.507** | | |
| **Commissure calcification** | **1.85 (0.99–3.45)** | **0.051** | | |
| **Eccentricity index** | **1.00 (0.96–1.05)** | **0.889** | | |




| | COV of OI | Sen | Spe | AUC (95% CI) | *P* value |
|---|---|---|---|---|---|
| Sapien system | 10.2% | 0.663 | 0.875 | 0.769 (0.628-0.909) | 0.001 |
| Evolut system | 17.6% | 0.552 | 0.711 | 0.639 (0.532-0.746) | 0.018 |

| | Multivariable Analysis | | | Multivariable Analysis | |
|---|---|---|---|---|---|
| **Valve without leakage-proof function** | **OR (95% CI)** | **P value** | **Valve with leakage-proof function** | **OR (95% CI)** | **P value** |
| **Total calcium amount >800** | 4.22 (1.52–11.71) | 0.006* | | | |
| **OI per a decrease by 5%** | 1.65 (1.19–2.28) | 0.003* | **OI per a decrease by 5%** | 2.983 (1.54–5.79) | 0.001* |
| | | | **Evolut / PRO vs Lotus/Sapien 3** | 27.67 (5.54–138.31) | <0.001* |
| | | | **(Evolut / PRO vs Sapien 3)** | 25.50 (4.49–144.75) | <0.001* |
| | | | **(Evolut / PRO vs Lotus)** | 34.48 (5.99–200.00) | <0.001* |

# Our routine practice

## TAVI Case preview
### CT angiography (20-02-11)

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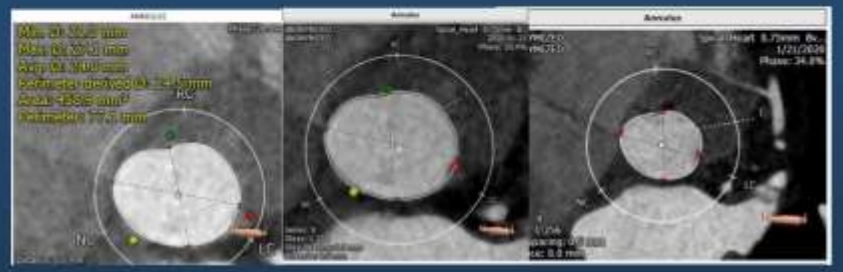
## TAVI Case preview
### Annulus measurement



| Medtronic | Edwards | Boston |
|---|---|---|
| Min diameter 21.0mm | Min diameter 21.9mm | Min diameter 21.8mm |
| Max diameter 27.1mm | Max diameter 27.4mm | Max diameter 26.8mm |
| AVG diameter 24.0mm | AVG diameter 24.6mm | AVG diameter 24.3mm |

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## TAVI Case preview
### Measurement of dimensions

| | TTE | CTCA | Edwards | Medtronic | Boston |
|---|---|---|---|---|---|
| Annulus | 19.0 | 22.91*27.00 (mean,24.9) | 21.9*27.4 (mean, 24.6) | 21.0*27.1 (mean, 24.0) | 21.8*26.8 (mean, 24.3) |
| Annulus perimeter | - | 77.96 | 78.3 | 77.1 | 77.2 |
| Annulus area | - | - | 476.6 | 458.9 | 463.1 |
| St juction/ annulus ratio | - | - | 1.16 | 1.18 | 1.21 |
| LVOT/ annulus ratio | - | - | 1.00 | 1.01 | 1.00 |
| Height of coronary os | - | Lt: 11.13 Rt: 12.44 | Lt: 11.0 Rt: 14.1 | Lt:11.5 Rt:13.5 | Lt:12.5 Rt:15.0 |
| St junction height | - | - | Lt: 18.6 Rt: 19.7 | Lt:19.0 Rt:17.2 | Lt:19.6 Rt:18.4 |
| Sinus of Valsalva | 30.0 | - | 31.5 | - | - |
| Sinotubular junction | 23.0 | 27.03 | 28.5 | 29.0 | 28.9 |
| Ascending aorta | 35.0 | 34.0 | - | 32.3 | 35.3 |

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## TAVI Case preview
### Measurement of dimensions (Medtronic)

| Diameter (mm) | 23 | 23.5 | 24 | 24.5 | 25 | 25.5 | 26 | 26.5 | 27 | 27.5 | 28 | 28.5 | 29 | 29.5 | 30 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Perimeter | 72.2 | 73.8 | 75.4 | 77.0 | 78.5 | 80.1 | 81.6 | 83.2 | 84.8 | 86.4 | 87.9 | 89.5 | 91.1 | 92.6 | 94.2 |
| EvR/Pro 23 | | | | | | | | | | | | | | | |
| EvR/Pro 26 | 13.0% | 10.6% | 8.3% | | | | | | | | | | | | |
| EvR/Pro 29 | 26.1% | 23.4% | 20.8% | 18.4% | 16.0% | 13.7% | 11.5% | 9.4% | 7.4% | | | | | | |
| EvR 34 | | | | | | | 30.8% | 28.3% | 25.9% | 23.6% | 21.5% | 19.3% | 17.2% | 15.3% | 13.3% |

Annulus perimeter = 77.1mm
Annulus diameter = 24.5mm

➡ *Evolut Pro 29mm*

18.4% oversizing
(perimeter annulus 기준)

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## TAVI Case preview
### Measurement of dimensions (Edwards)

Annulus area = 476.6 mm²
Area driven diameter = 24.6mm

➡ *Sapien-3 26mm*

+1.0cc : 13.6%
+0.5cc : 11.3%
Nominal : 8.9%

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## TAVI Case preview
### Measurement of dimensions (boston)

| 구종태 | Patient | Lotus 25mm size | Difference | Oversize % |
|---|---|---|---|---|
| Area derived (mm) | 24.3 | 25 | -0.7 | 2.9% |
| Perimeter derived (mm) | 24.6 | 25 | -0.4 | 1.6% |

Annulus area = 463.1 mm²
Area driven diameter = 24.3mm

➡ *Lotus Edge 25mm*

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# How can we reduce (prevent) PVL ?

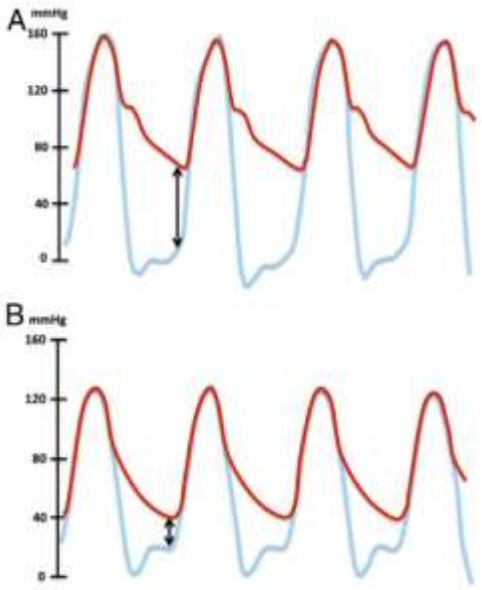
#1. Adequate Valve selection and sizing

#2. Precise evaluation and management

# How can we assess AR

- **AR index:** A simple, reproducible, and point-of-care assessment of periAR during TAVI

- Patients (N=146) who underwent TAVI with CoreValve Prosthesis
- Primary End point: 1 year all-cause mortality




AR index = [DBP-LVEDP] / SBP) * 100

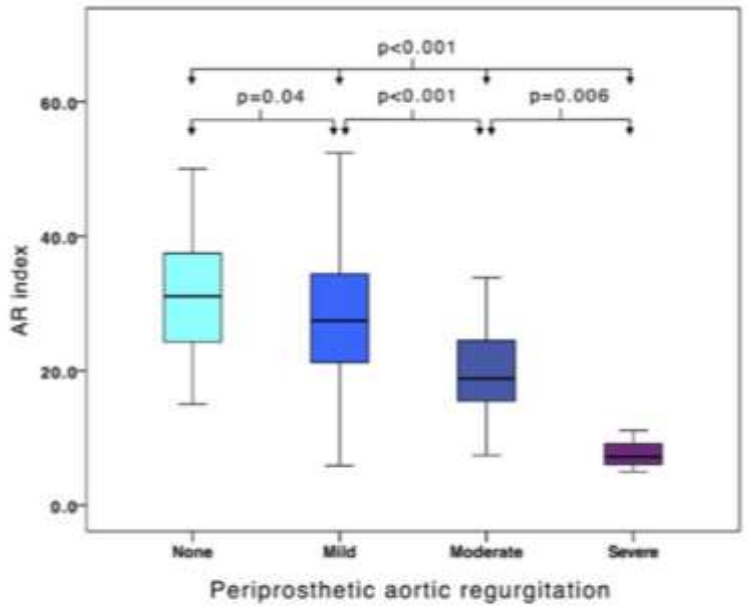



**Figure 2** **AR Index According to Degree of PeriAR**

The AR index according to the degree of periAR as assessed by echocardiography after transcatheter aortic valve implantation. Abbreviations as in Figure 1.

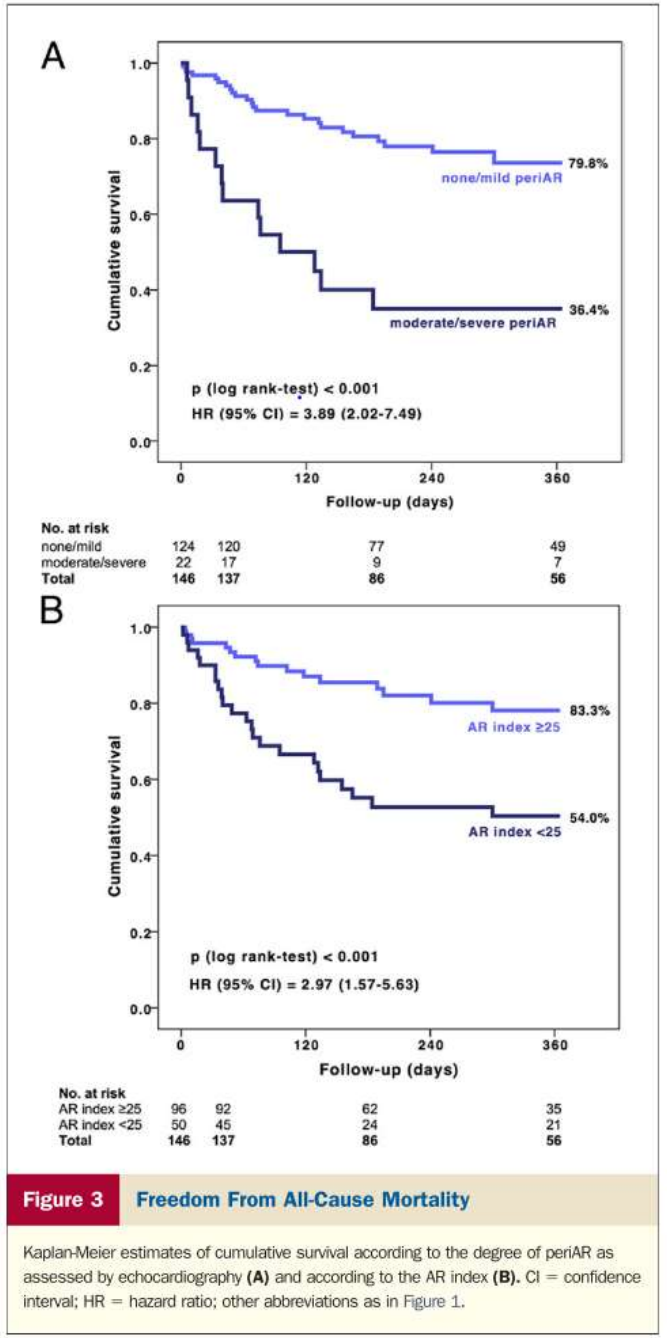



**Figure 3** **Freedom From All-Cause Mortality**

Kaplan-Meier estimates of cumulative survival according to the degree of periAR as assessed by echocardiography **(A)** and according to the AR index **(B).** CI = confidence interval; HR = hazard ratio; other abbreviations as in Figure 1.

Sinning, J.M., et al., J Am Coll Cardiol, 2012

# How can we assess AR

- **Is the AR index Too simple?**
  - Time-integrated aortic regurgitation (TIAR) index
    - [LV - Ao diastolic pressure time integral] / [LV systolic pressure time integral] × 100.

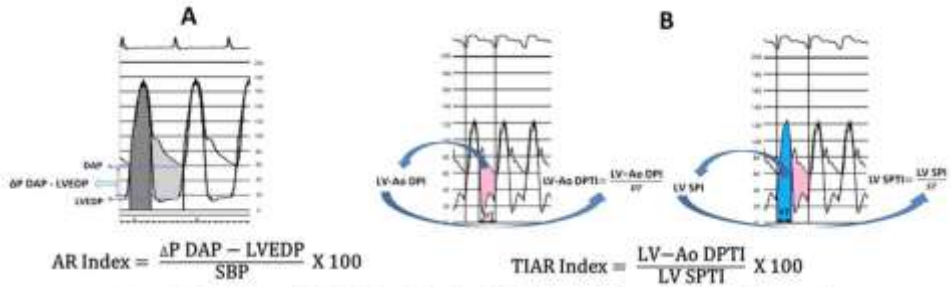
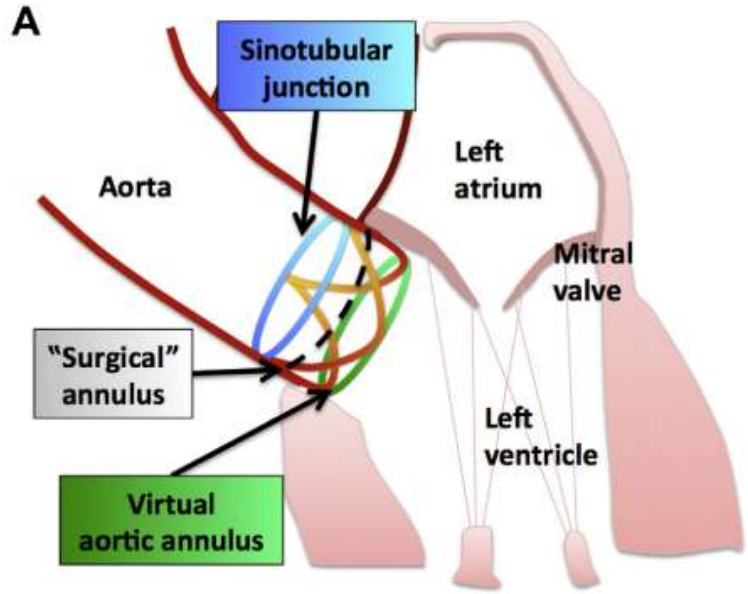



Fig. 1. Calculation of the AR index (A) and the TIAR index (B). Ao, aortic; AR, aortic regurgitation; DAP, diastolic aortic pressure; DPI, diastolic pressure integral; DPTI, diastolic pressure time integral; DT, diastolic time; LV, left ventricular; LVEDP, left ventricular end-diastolic pressure; SBP, systolic blood pressure; SPI, systolic pressure integral; SPTI, systolic pressure time integral; ST, systolic time; TIAR, time-integrated aortic regurgitation.

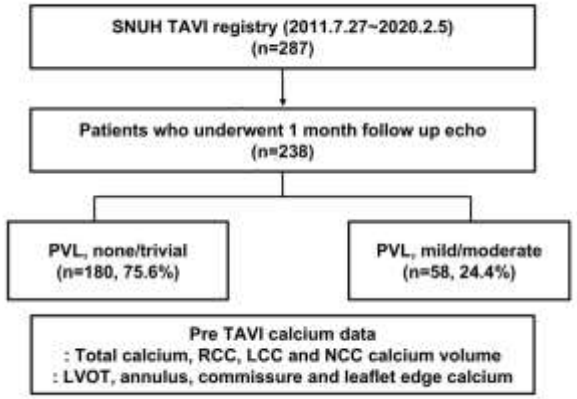
- **A New AR index is needed**
  - The "pressure drop" is related to AR
  - The diastolic hemodynamics is associated with ***HR, atrial function, rhythmic problems, myocardial stiffness, mitral valvular status***, which influence the interval of diastole.

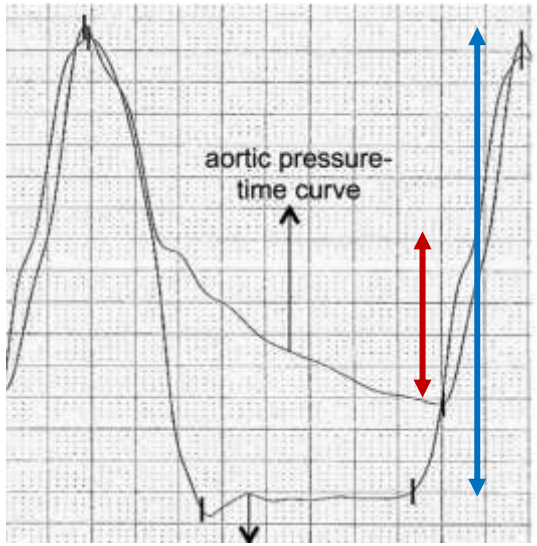


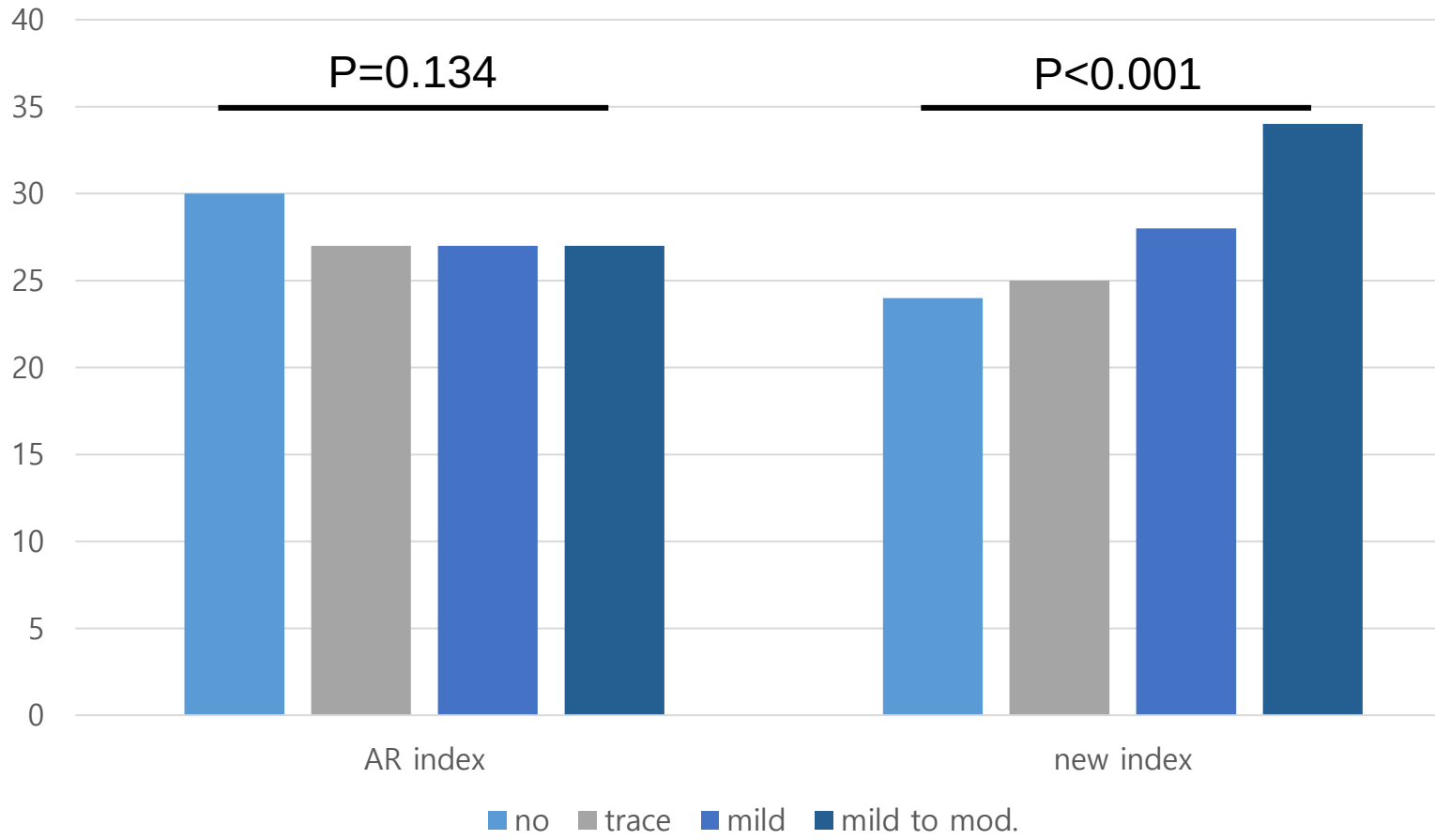

Bugan, B., et al., Catheter Cardiovasc Interv, 2015

# Balance between simple and inaccessible

- The Dicrotic AR index
  - [ (AoSBP) – (LVEDP) ] / [(dicrotic notch pressure) - (AoDBP) ] * 100



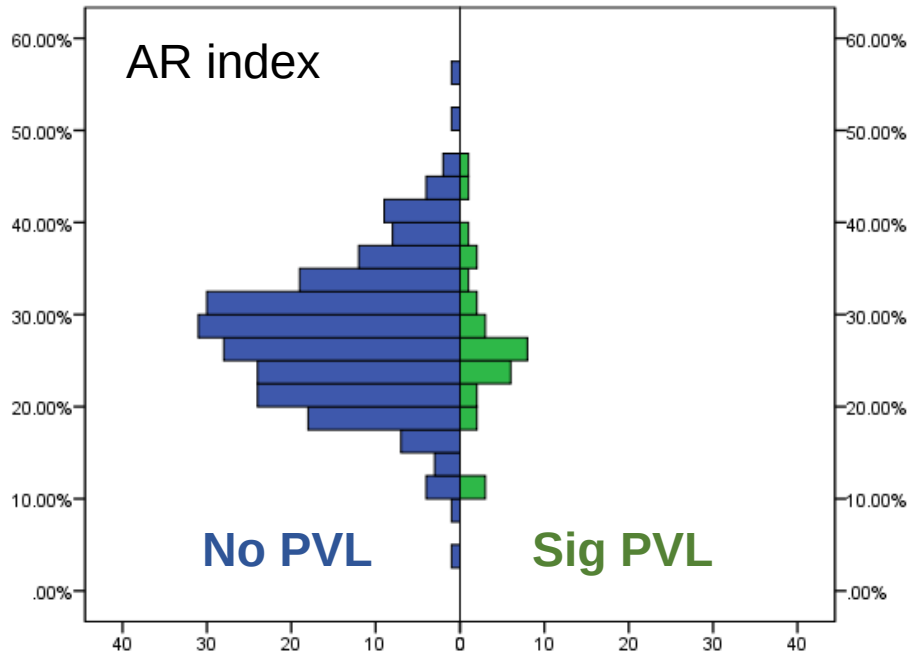



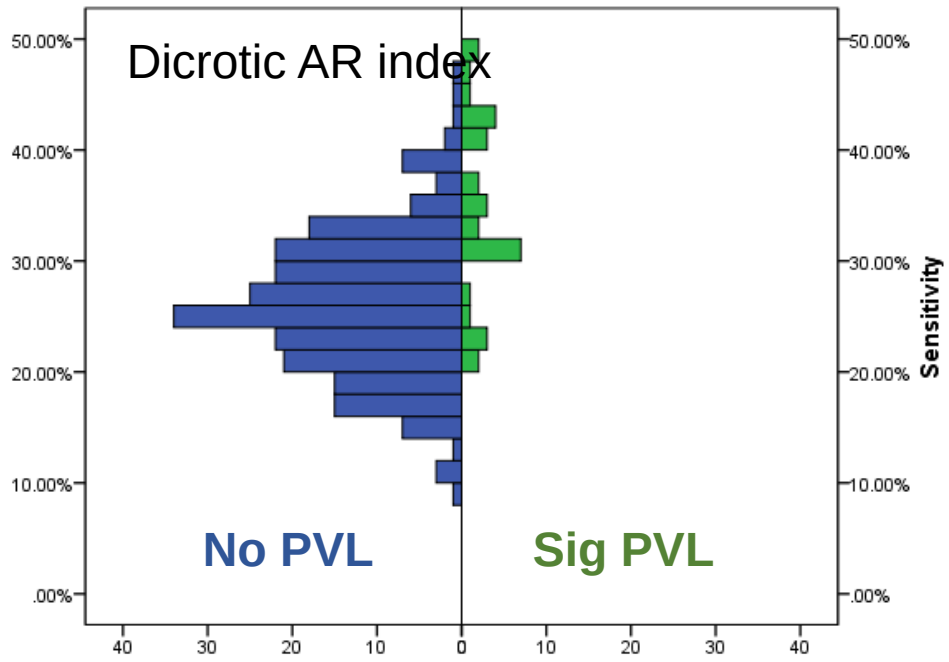

J Kang et al, JACC cardiovasc interv. 2020

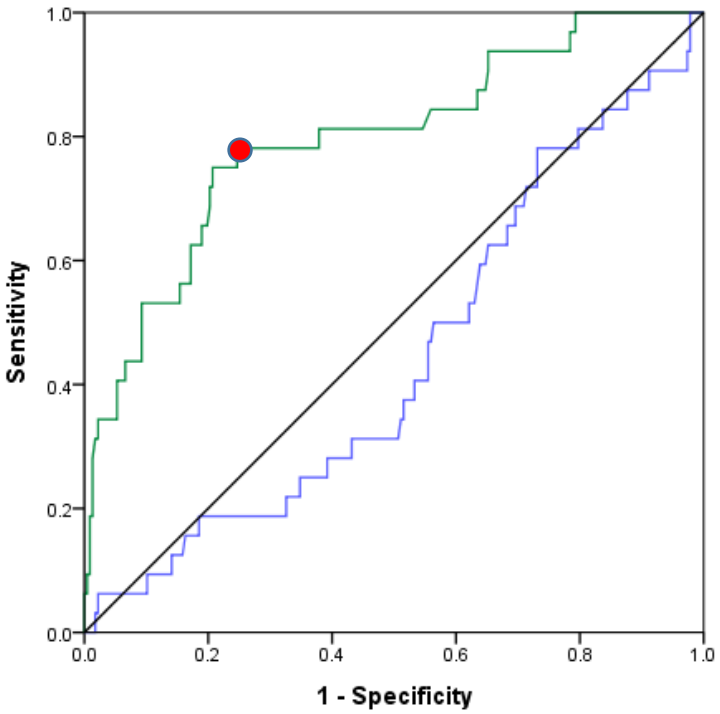
# Dicrotic AR index

- [ (AoSBP) – (LVEDP) ] / [(dicrotic notch pressure) - (AoDBP) ] * 100
  - AR index
    - AUC 0.444 (0.340-0.547), p=0.303
  - Dicrotic AR index
    - AUC 0.795 (0.706-0.885), p<0.001

Best cutoff value
newARindex = 3.3
Sensitivity 78%, Specificity 75%




J Kang et al, JACC cardiovasc interv. 2020

# Example Case

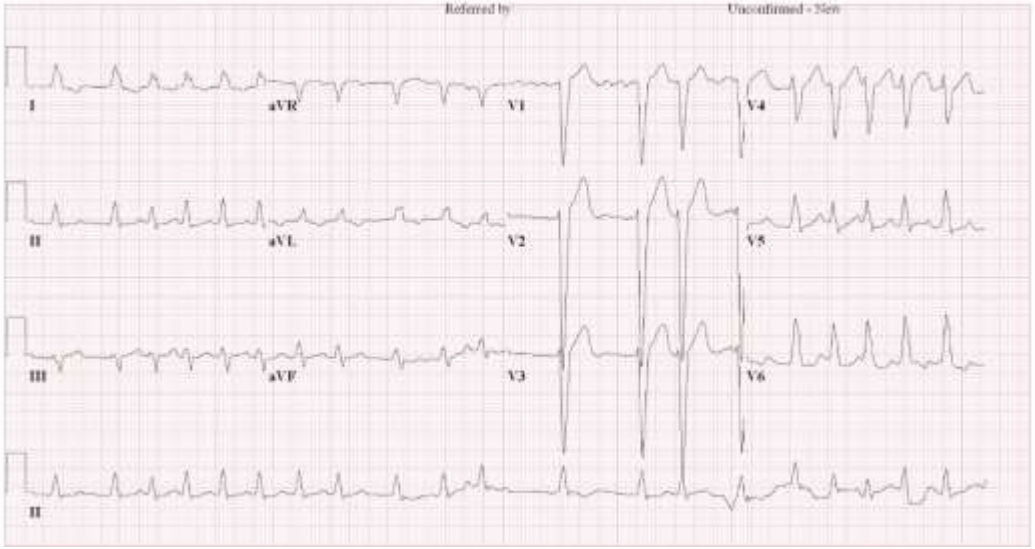
- 79/F

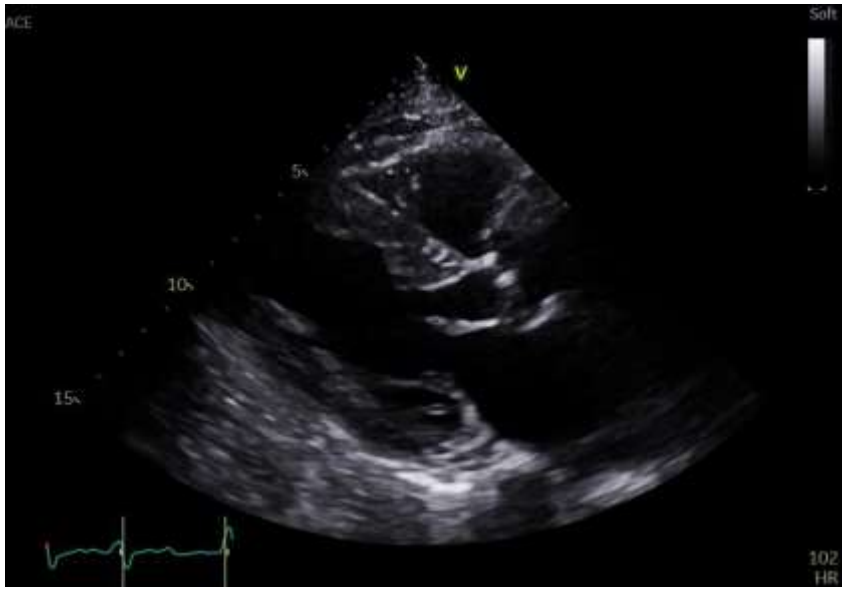
# Severe AS

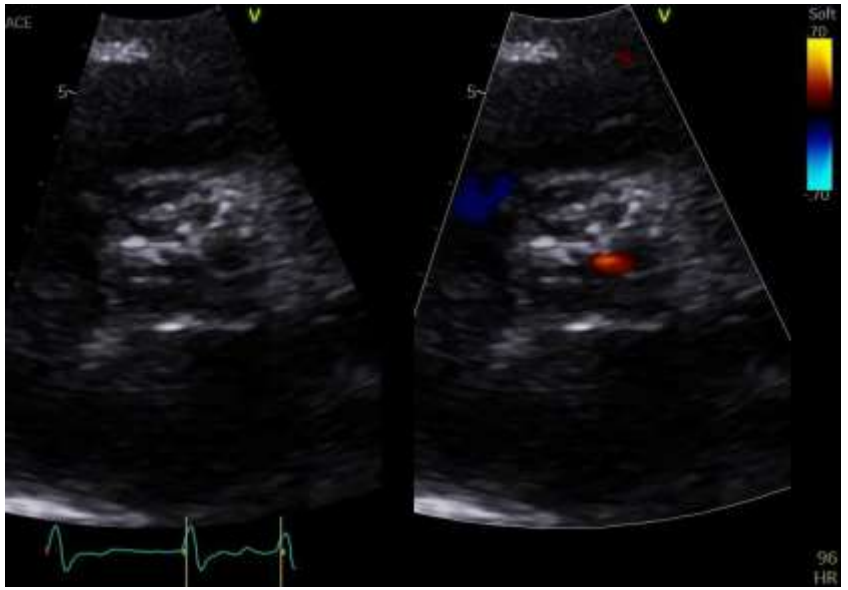
# DM(Dx'ed '02)  / HTN

# CHF d/t IHD (NYHA Fc III)

# AF on apixaban ('20.2~)

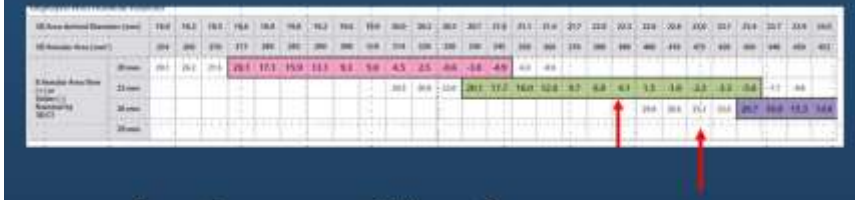




# Example Case

## TAVI Case preview
## Measurement of dimensions (Edwards)



Annulus area = 415 mm²
Area driven diameter = 23.0 mm

➡ *Sapien-3 26mm*

Nominal : 24.8%
-2.0cc : 14.2%
-2.5cc : 11.5%

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## TAVI Case preview
## Measurement of dimensions (Medtronic)

| Diameter (mm) | 23 | 23.5 | 24 | 24.5 | 25 | 25.5 | 26 | 26.5 | 27 | 27.5 | 28 | 28.5 | 29 | 29.5 | 30 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Perimeter | 72.2 | 73.8 | 75.4 | 76.9 | 78.5 | 80.1 | 81.6 | 83.2 | 84.8 | 86.4 | 87.9 | 89.5 | 91.1 | 92.6 | 94.2 |
| EvR/Pro 23 | | | | | | | | | | | | | | | |
| EvR/Pro 26 | 13.0% | 10.6% | 8.3% | | | | | | | | | | | | |
| EvR/Pro 29 | 26.1% | 23.4% | 20.8% | 18.4% | 16.0% | 13.7% | 11.5% | 9.4% | 7.4% | | | | | | |
| EvR 34 | | | | | | | 30.8% | 28.3% | 25.9% | 23.6% | 21.5% | 19.3% | 17.2% | 15.3% | 13.3% |

Annulus perimeter = 74.9mm
Annulus diameter = 23.9mm

➡ *Evolut Pro 29mm*

21.3% oversizing
(annulus perimeter 기준)

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## TAVI Case preview
## Measurement of dimensions (boston)

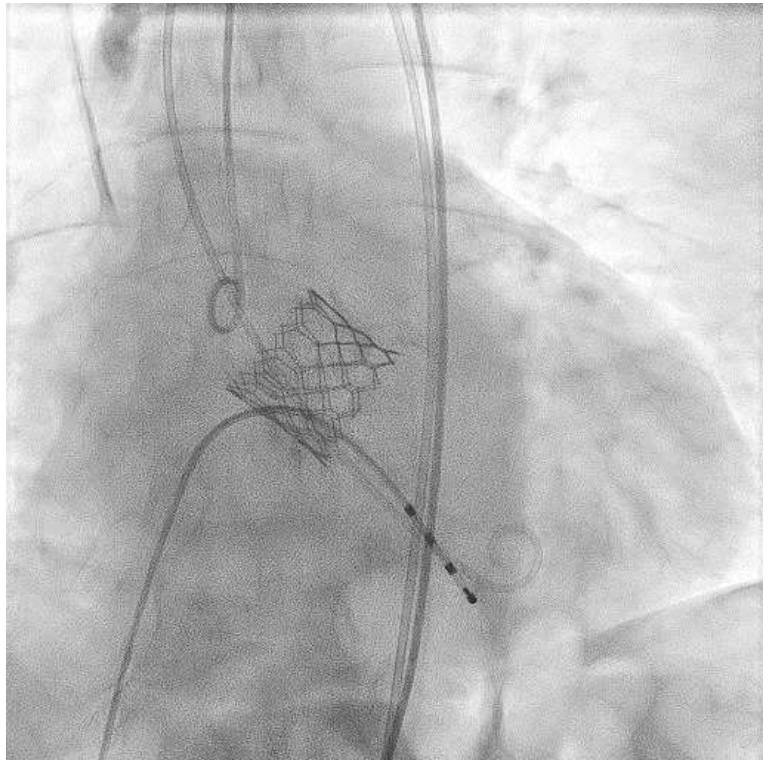
| 이름순 | Patient | Lotus 25mm size | Difference | Oversize % |
|---|---|---|---|---|
| Area derived (mm) | 23.1 | 25 | -1.9 | 8.2% |
| Perimeter derived (mm) | 23.9 | 25 | -1.1 | 4.6% |

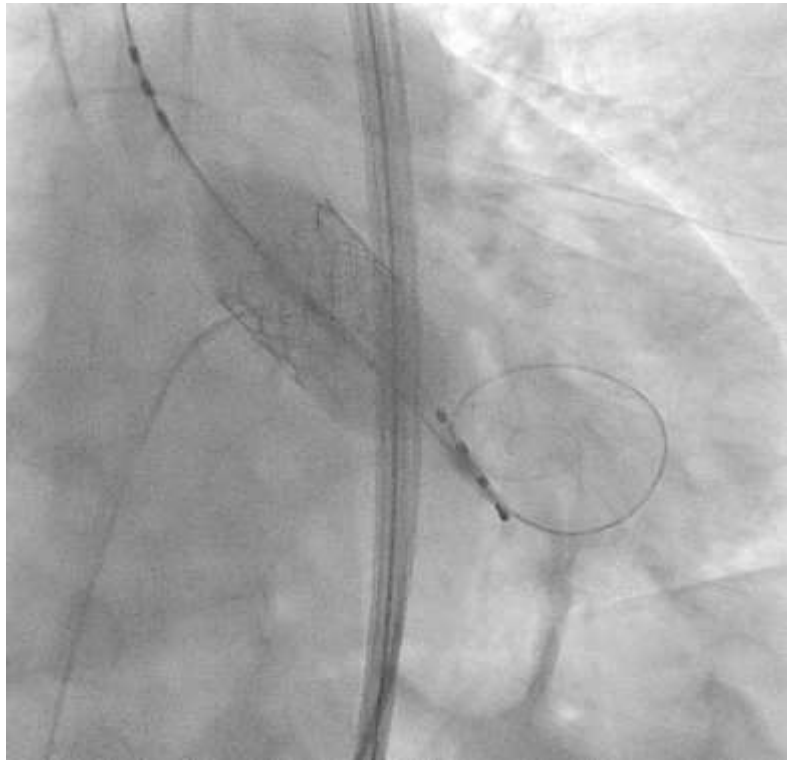
Annulus area = 420.8 mm²
Area driven diameter = 23.9mm

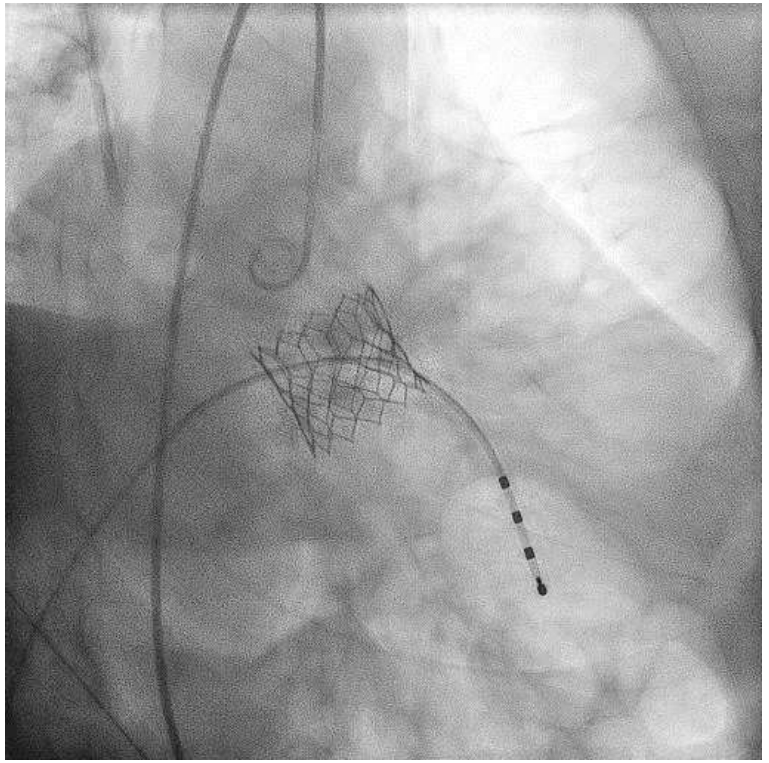
➡ *Lotus Edge 25mm*

Seoul National University Hospital Cardiovascular Center

# Example Case





| | Initial |
|---|---|
| AR index | 29.0 |
| Dicrotic AR index | 2.6 |

| | Initial |
|---|---|
| AR index | 27.3 |
| Dicrotic AR index | 3.7 |

# Conclusion

- ✓ TAVI is expanding…

- ✓ Now we need ***fine tuning*** to accelerate and reinforce TAVI as a standard
  - ✓ Not more an alternative of SAVR
  - ✓ More delicate pre-evaluation, More standardization, More optimization needed.

- ✓ We suggest 2 new in indexes that can be used for ***optimization***
  - ✓ ***Oversizing index*** : to select the adequate valve and inflation method
  - ✓ ***Dicrotic AR index*** : to evaluate AR and guide adjunctive therapy