Impact of Renin-Angiotensin System inhibition in patients following Transcatheter Aortic Valve Implantation: The multicenter RASTAVI study.

ClinicalTrials.gov ID: NCT03201185

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Potential conflicts of interest

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☑ I have no potential conflicts of interest to report

Why this study?

- Several studies have demonstrated the benefits of transcatheter aortic valve implantation (TAVI) in aortic stenosis (AS) patients
- However, the presence of persistent myocardial **fibrosis** and **hypertrophy** has been related to worse prognosis[1]
- Therefore, we aimed to explore the potential benefits of renin-angiotensin system inhibitors (**RASi**) on left ventricular remodeling and major clinical outcomes following successful TAVI

[1]Magne J, et al. Am J Cardiol. 2018;121:455-60.

What did we study?

- Patients from 10 institutions with severe AS who underwent TAVI between August/2007 and August/2017 were included. All baseline data were prospectively recorded and pre-specified follow up was performed.
- Dose and type of RASi at discharge were recorded and matched comparison according to its prescription at discharge was performed.

Primary endpoint	Secondary endpoint
Clinical outcomes at short- and mid-term follow-up (3-year), according to the prescription or not of RASi at discharge	**Echocardiographic changes** at short- and mid-term follow-up (3-year), according to the prescription or not of RASi at discharge

Where was the study executed?

Center location

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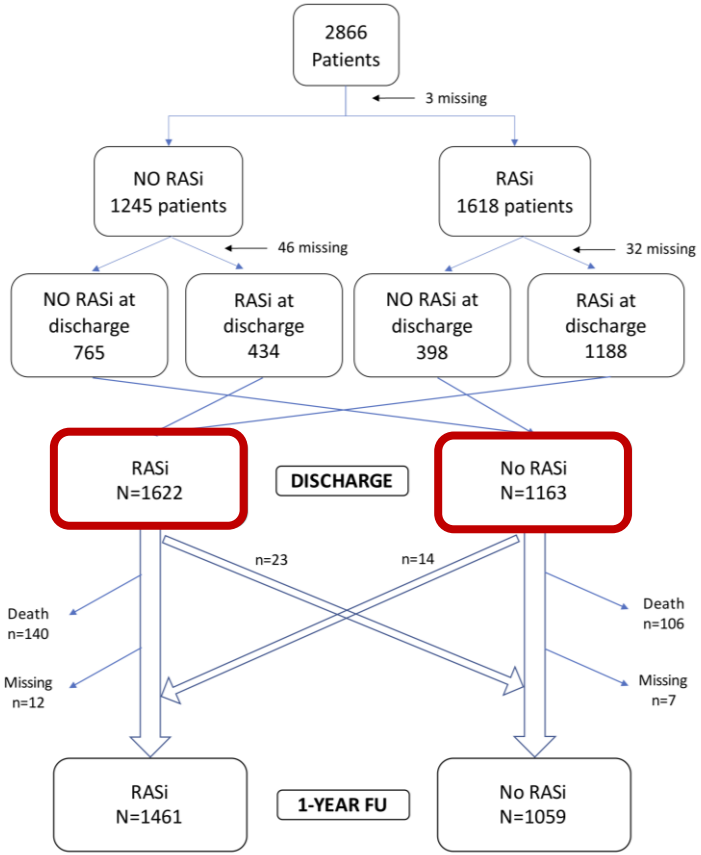
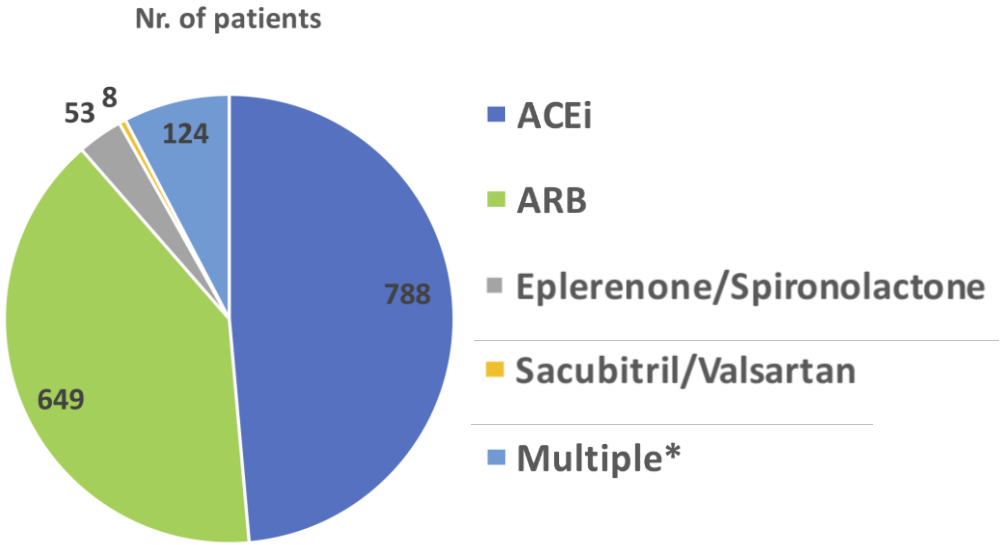
How was the study executed?

- **Observational, retrospective** registry at 10 sites in Spain & Brazil with **2785 pts** divided into 2 groups after TAVI according to the use of RASi at discharge
- **TTE:** baseline, discharge and follow-up and centrally analysed
- **Propensity score (PS) adjustment** including: age, chronic kidney disease, chronic obstructive pulmonary disease, coronary artery disease, diabetes mellitus, dislipemia, hypertension, LV ejection fraction, and NYHA class. Pairs of patients were derived using greedy 1:1 with a calliper width of 0.25 SD of the logit of PS.
- **Kaplan-Meier analysis** according to the use of RASi
- **Cox multivariable regression analysis** was performed to identify the independent predictors of global and cardiovascular mortality in the matched population

How was the study executed?





What are the essential results?

Baseline characteristics

Variables	Matched population		
	RASi (n=695)	No-RASi (n=695)	p-value
Age, years	80.8±6.9	80.6±7.4	0.644
Female sex	373(53.7)	374(53.8)	0.957
Hypertension	545(78.4)	542(78.0)	0.845
Diabetes mellitus	232(33.4)	246(35.4)	0.429
NYHA functional class III or IV	464(66.8)	472(67.9)	0.647
Atrial fibrillation	225(32.4)	222(31.9)	0.863
Previous MI	110(15.8)	108(15.5)	0.883
CKD (eGFR<60ml/min)	291(41.9)	298(42.9)	0.704
EuroScore II (%)	4.1[2.9-6.9]	4.1[2.8-6.8]	0.887
Left ventricular ejection fraction, %	58.5±13.9	58.1±13.7	0.544
Mean transaortic gradient, mmHg	47.9±15.3	48.9±17.6	0.255
End-diastolic volume, cc	99[80-113]	99[79-113]	0.359
Septal hypertrophy, mm	14.7±4.8	15.2±5.4	0.140

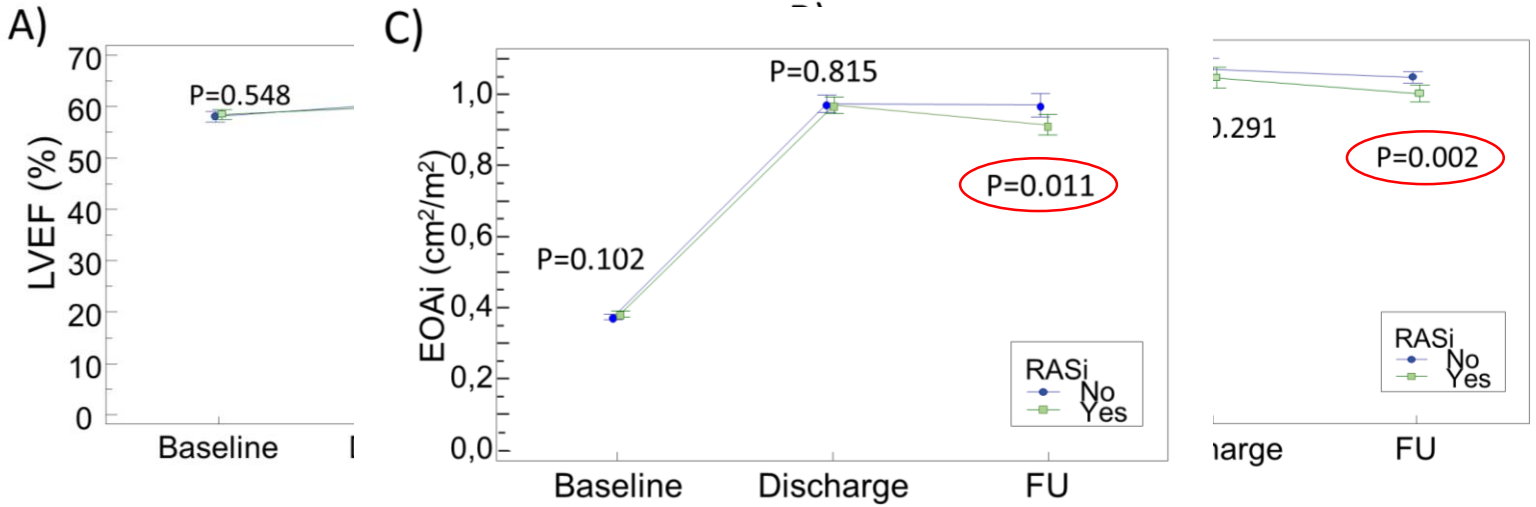
What are the essential results?

Echocardiographic Outcomes (3-yr FU)

LVEF

EOAi

LV Hypertrophy



What are the essential results?

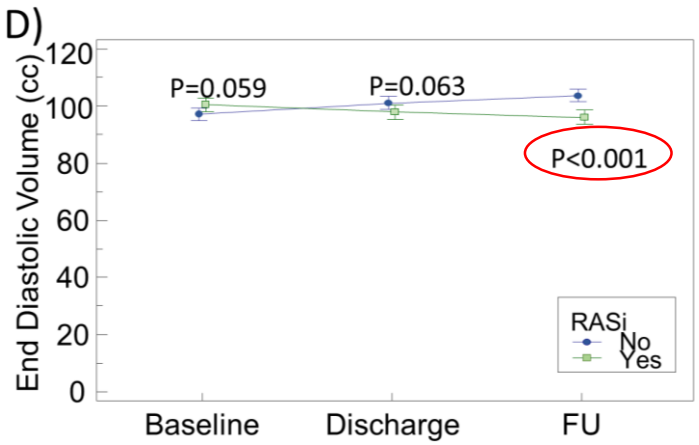
Changes in echocardiographic parameters from baseline to follow up

Variables	Matched population		
	RASi (n=695)	No-RASi (n=695)	P
Δ Left ventricular ejection fraction, %	0 [-5, 9]	2 [-5, 10]	0.076
Δ Aortic valve area, cm^2	0.90 [0.6, 1.2]	1.0 [0.73, 1.3]	**0.008**
Δ Mean transaortic gradient, mm Hg	-36.8 [-47, -28]	-37 [-48, -29]	0.264
Δ Telediastolic volume, cc	-10 [-10, 6]	4 [4, 11]	**<0.001**
Δ Telesystolic volume, cc	1 [1, 4]	4 [3, 8]	**<0.001**
Δ Septal hypertrophy, mm	-3 [-3, 0]	0 [0, 1]	**<0.001**

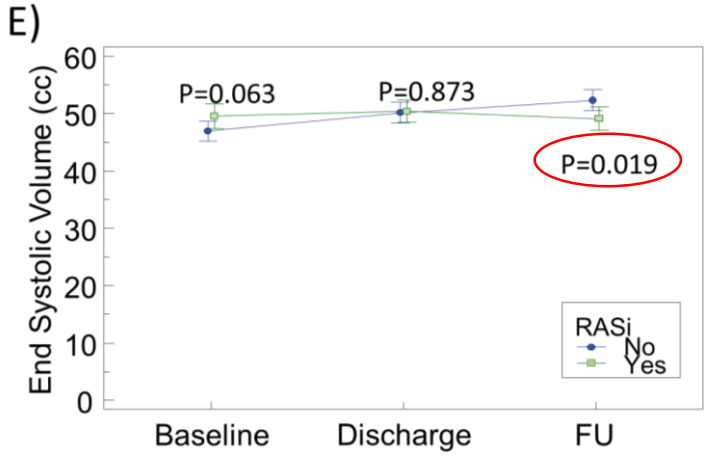
What are the essential results?

Echocardiographic Outcomes (3-yr FU)

End-Diastolic LV volume



End-Systolic LV volume



What are the essential CLINICAL results?

Main Outcomes (3-yr FU)

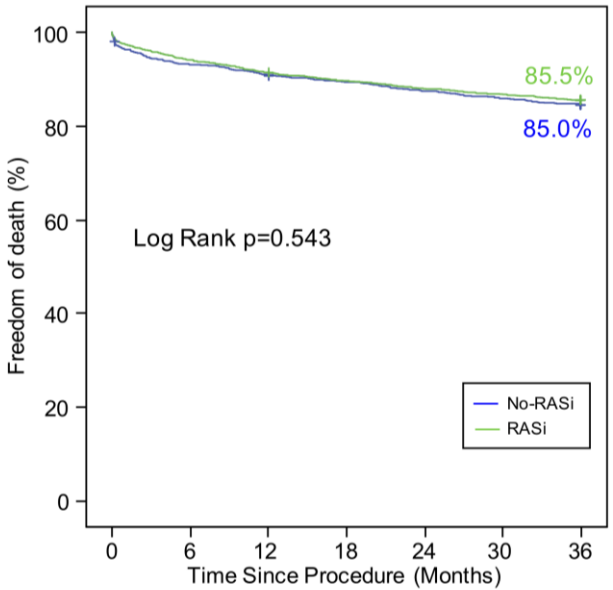
Variables	Matched population		
	RASi (n=695)	No-RASi (n=695)	P
New onset atrial fibrillation	23.2%	32%	**0.002**
Stroke/TIA	1.4%	5.9%	**<0.001**
Readmission	42.8%	51.9%	**0.017**
Cardiac readmission	52.8%	63%	0.066
NYHA class III-IV	13.8%	10.1%	0.112
All-Cause mortality	18.4%	19.6%	0.567
Cardiovascular mortality	7.2%	11.3%	**0.006**

What are the essential CLINICAL results?

UNMATCHED

Global mortality

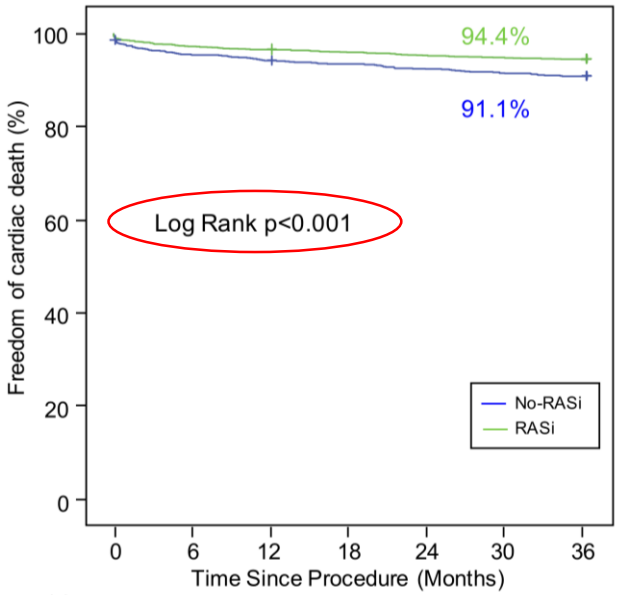
Mortality 3 year	No-RASi	RASi
412	177	235



Patiens at risk							
No-RASi	1160	1080	1054	1034	1012	994	980
RASi	1621	1526	1482	1453	1426	1407	1385

Cardiovascular mortality

Cardiac mortality 3 year	No-RASi	RASi
197	107	90



Patients at risk							
No-RASi	1156	1079	1053	1034	1012	994	980
RASi	1620	1526	1482	1453	1426	1407	1385

UNMATCHED

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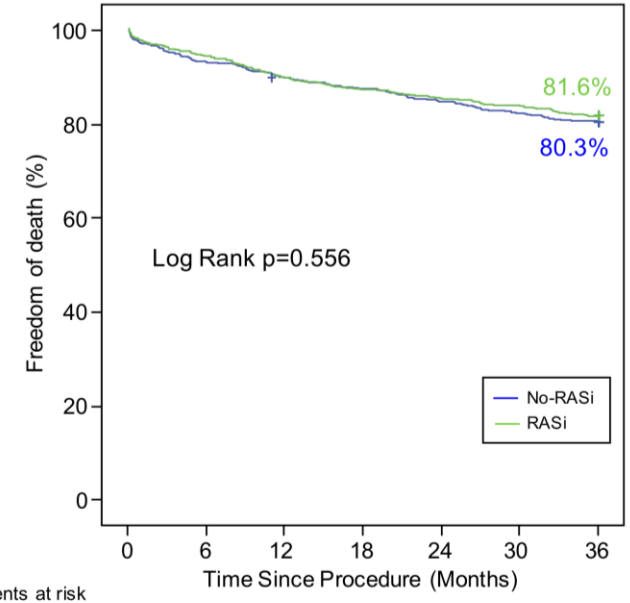
What are the essential CLINICAL results?

Global mortality

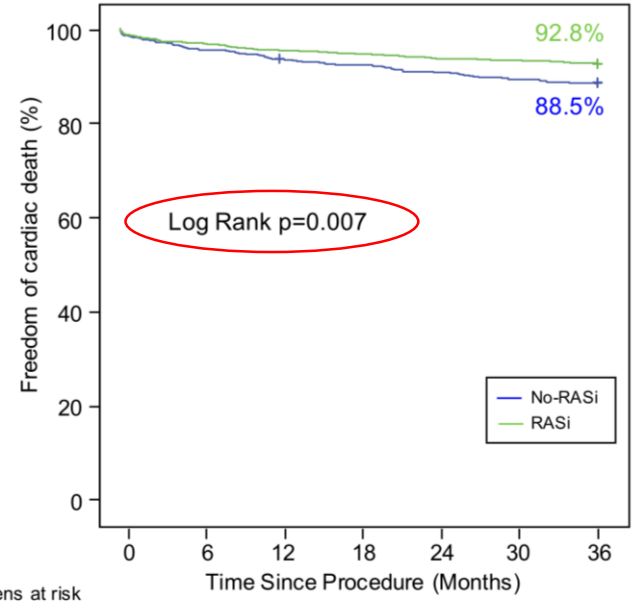
Mortality 3 year	No-RASi	RASi
264	136	128



Patients at risk							
No-RASi	693	644	621	603	584	567	555
RASi	695	655	623	606	593	583	567

Cardiovascular mortality

Cardiac mortality 3 year	No-RASi	RASi
129	79	50



Patiens at risk							
No-RASi	690	643	620	603	584	567	555
RASi	695	655	623	606	593	583	567

MATCHED

MATCHED

What are the essential results?

Main predictors of cardiovascular mortality

Variables	Univariate HR (95% CI)	P	Multivariate HR (95% CI)	P
CAD	1.49 (1.06-2.12)	0.022		
Previous PCI	1.85 (1.29-2.65)	0.001	1.98 (1.35-2.91)	<0.001
CKD	1.69 (1.20-2.40)	0.003		
COPD	1.63 (1.13-2.35)	0.009	1.49 (1.01-2.21)	0.049
Prior Stroke/TIA	1.65 (1.06-2.58)	0.026		
Baseline NYHA III-IV	2.19 (1.41-3.41)	0.001	1.82 (1.13-2.91)	0.013
Hypertension	1.78 (1.08-2.93)	0.023		
Post-TAVI CVE	5.28 (2.97-9.38)	<0.001	5.29 (2.87-9.72)	<0.001
NOAF	2.31 (1.42-4.31)	0.008		
Post-TAVI Ao.Reg. III-IV	3.18 (1.49-6.83)	0.003	3.77 (1.73-8.21)	0.001
RASi at discharge	0.62 (0.43-0.89)	0.008	0.59 (0.41-0.87)	0.007

Why is this important?

- Irrespective of baseline differences, RASi following TAVI were associated with:
  - **Lower rate of cardiac mortality** at short- and mid-term follow up.
  - **Global cardiovascular protective effect** – lesser Afib and CVE –.
- The improved clinical outcomes in patients under RASi might, at least in part, be mediated by a left ventricular **positive remodeling**
- An ongoing RCT (RASTAVI Study, NCT03201185) will help to corroborate these hypotheses-generating findings

RASTAVI – Retrospective Cohort

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The essentials to remember

WHY?

- The presence of persistent myocardial fibrosis / hypertrophy has been related to worse prognosis after TAVI

WHAT?

- 2785 pts divided into 2 groups after TAVI according to the use of RASi at discharge in 10 centers with 3-year follow up and echocardiographic central analysis. Matched comparison (n=695 for each group).

HOW?

- The primary endpoint was MACE at 3-year follow up according to the prescription or not of RASi at discharge
- The secondary endpoint was the variation in echocardiographic parameters at 3-year follow up , according to the prescription or not of RASi at discharge

WHAT ARE THE RESULTS ?

- RASi were associated with lower cardiovascular mortality rate irrespective of baseline differences
- A global cardiovascular protective effect was suggested by lower rate of AFib and cerebrovascular events
- This effect can be partially explained by a more favorable remodeling of the LV in patients under RASi

WHY IS IT IMPORTANT?

- If confirmed in the RASTAVI RCT, these findings might suggest the need for systematic use of RASi after TAVI