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XXXIII.

VÝROČNÍ SJEZD
ČESKÉ KARDIOLOGICKÉ
SPOLEČNOSTI

EARLY TAVR

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Transcatheter Aortic-Valve Replacement for Asymptomatic Severe Aortic Stenosis

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- Design studie:
  - prospektivní, multicentrická, otevřená, randomizovaná studie , USA + Kanada
- Studijní populace:
  - pacienti s významnou, asymptomatickou aortální stenózou
- Randomizace:
  - TAVI vs. konzervativní léčba do nástupu symptomů
- Intervence:
  - Implantace balón-expandabilní chlopně Edwards Sapien 3, nebo Edwards Sapien 3 Ultra
- Primární cíl:
  - Kombinovaný cíl – celková mortalita, CMP, neplánovaná hospitalizace z kardiální příčiny

Inclusion Criteria

Patients must meet the following inclusion criteria to be included in the trial:

1. 65 years of age or older at time of randomization
2. Severe aortic stenosis defined as:
    a. Aortic valve area (AVA) ≤1.0 cm2 **or** AVA index ≤0.6 cm2/m2 **AND**
    b. Peak jet velocity ≥4.0 m/s **or** Mean gradient ≥40 mmHg
3. Patient is asymptomatic defined as:
    a. Negative treadmill stress test. To be considered asymptomatic, the patient must not demonstrate any of the following during and/or after the test:
        i. Syncopal or pre-syncopal episode, including severe dizziness
        ii. Angina
        iii. Limiting dyspnea or decreased exercise tolerance, defined as inability to reach 60% of age and sex adjusted metabolic equivalents of task (METs)
        iv. Drop in systolic blood pressure (defined as a progressive drop of at least 20 mmHg and sustained for 1 minute or an acute drop of 40 mmHg)[1]
        v. Significant ventricular arrhythmias (≥4 consecutive ventricular premature beats)

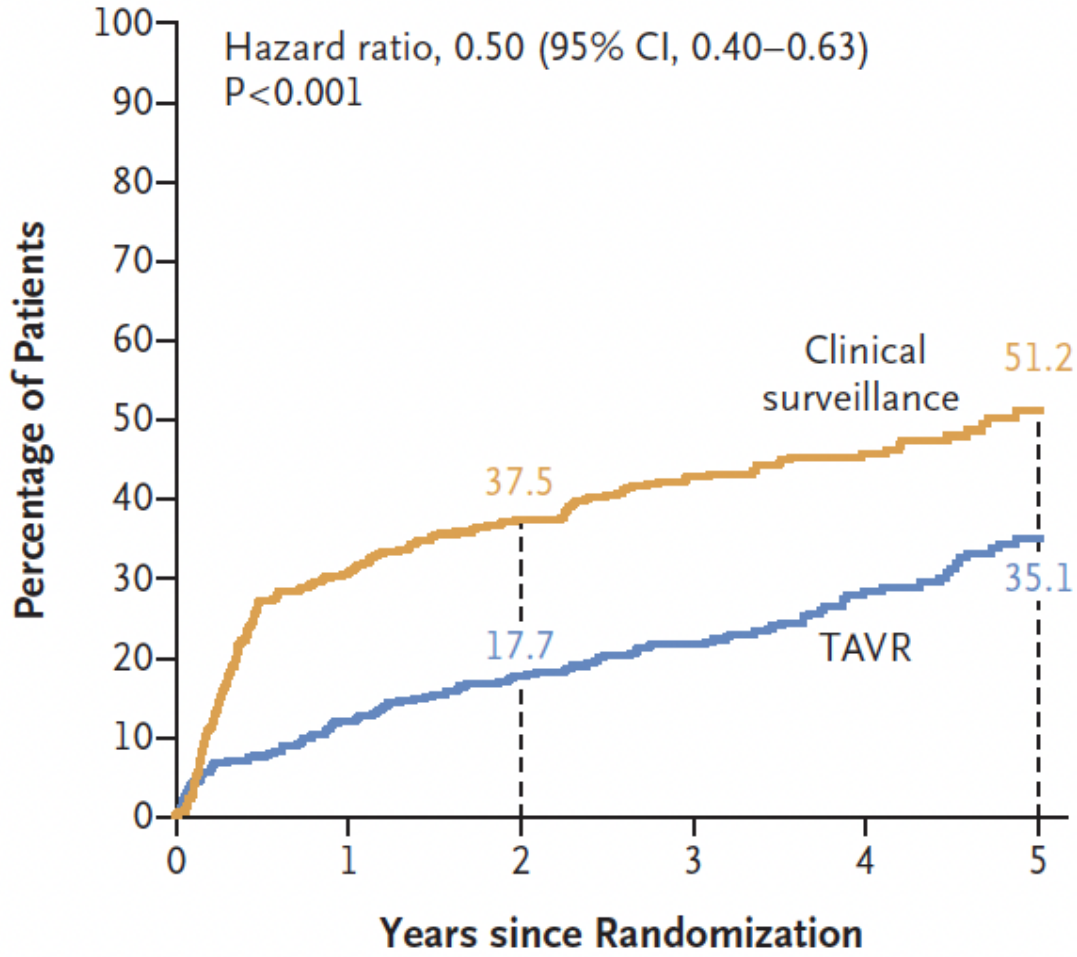
    OR

    b. Per physician after thorough assessment of patient history if the patient is unable to perform a stress test.
4. Left ventricular (LV) ejection fraction ≥50%
5. Society of Thoracic Surgeons (STS) risk score ≤10
6. The study patient has been informed of the nature of the study, agrees to its provisions and has provided written informed consent as approved by the institutional review board of the respective clinical site.

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	TAVR (N=455)	Clinical Surveillance (N=446)
Age — yr	76.0±6.0	75.6±6.0
Female sex — no. (%)	131 (28.8)	147 (33.0)
Race — no. (%)†		
White	436 (95.8)	422 (94.6)
Black	9 (2.0)	11 (2.5)
Asian	7 (1.5)	9 (2.0)
Multiple or unknown	3 (0.7)	4 (0.9)
Hispanic or Latino ethnic group†	11 (2.4)	9 (2.0)
Body-mass index‡	28.4±4.6	28.6±4.8
STS-PROM score — %§	1.8±1.0	1.7±1.0
Able to perform treadmill stress test — no. (%)¶	411 (90.3)	405 (90.8)
Median NT-proBNP level (IQR) — pg/ml**	275.6 (138.8–598.9)	296.8 (147.6–607.7)
Bicuspid aortic valve on computed tomography — no./total no. (%)	37/455 (8.1)	39/444 (8.8)
Echocardiographic core laboratory variables		
Aortic-valve peak velocity — m/sec††	4.3±0.5	4.4±0.4
Mean transaortic gradient — mm Hg‡‡	46.5±10.1	47.3±10.6
Aortic-valve area — cm^2§§	0.9±0.2	0.8±0.2
Left ventricular ejection fraction — %¶¶	67.4±6.5	67.4±6.7

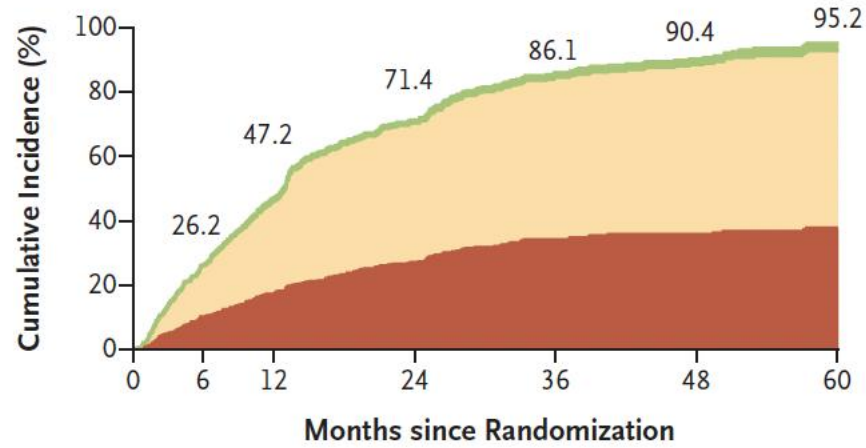
A Death, Stroke, or Unplanned Hospitalization for Cardiovascular Causes (%)



No. at Risk

TAVR	455	390	363	285	142	103
Clinical surveillance	446	305	266	187	117	46

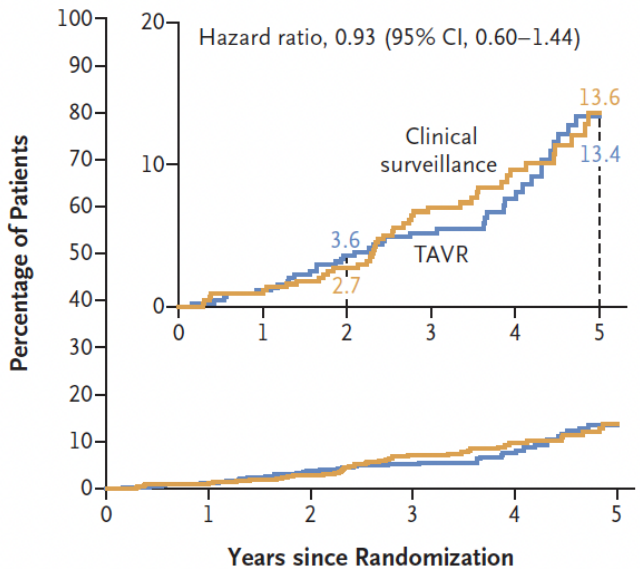
B Conversion to Aortic-Valve Replacement



No. at Risk

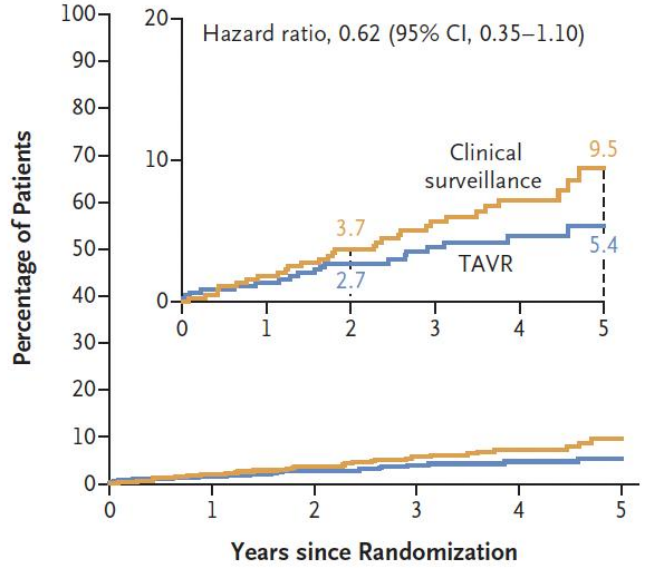
Clinical surveillance	446	326	231	119	45	22	9

B Death from Any Cause



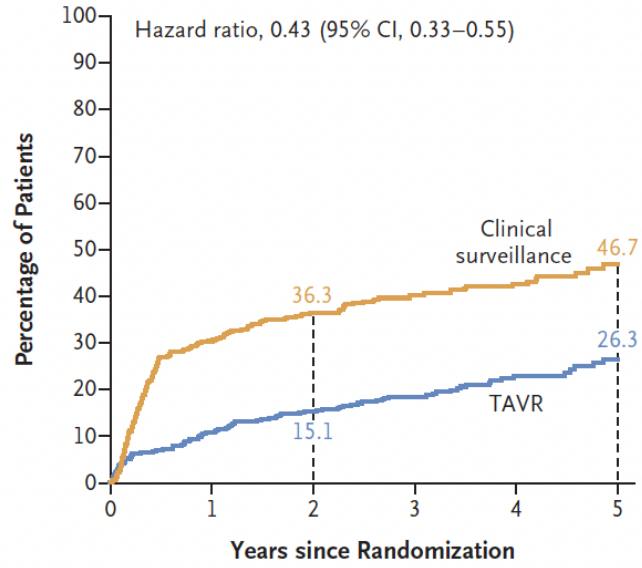
No. at Risk						
TAVR	455	439	425	346	187	136
Clinical surveillance	446	436	418	310	199	95

C Stroke



No. at Risk						
TAVR	455	433	415	335	180	130
Clinical surveillance	446	429	406	295	185	87

D Unplanned Hospitalization for Cardiovascular Causes



No. at Risk						
TAVR	455	392	365	287	142	103
Clinical surveillance	446	306	267	189	118	46

Table 2. Primary and Secondary End Points.*

End Point	TAVR (N=455)	Clinical Surveillance (N=446)	Treatment Effect (95% CI)†	P Value‡
Primary end point				
Composite of death, stroke, or unplanned hospitalization for CV causes — no. (%)§	122 (26.8)	202 (45.3)	0.50 (0.40 to 0.63)	<0.001
Death	38 (8.4)	41 (9.2)	0.93 (0.60 to 1.44)	—
Stroke	19 (4.2)	30 (6.7)	0.62 (0.35 to 1.10)	—
Unplanned hospitalization for CV causes§	95 (20.9)	186 (41.7)	0.43 (0.33 to 0.55)	—
Secondary end points				
Favorable outcome at 2 yr — no./total no. (%)¶	354/409 (86.6)	266/391 (68.0)	18.5 (12.6 to 24.3)	<0.001
Alive	425/441 (96.4)	418/430 (97.2)	—	—
KCCQ score ≥75	373/395 (94.4)	313/390 (80.3)	—	—
KCCQ score decrease of ≤10 from baseline	356/392 (90.8)	281/387 (72.6)	—	—
Integrated measures of LV and LA health at 2 yr — no./total no. (%)‖	180/374 (48.1)	121/337 (35.9)	12.2 (4.4 to 19.4)	0.001
LV global longitudinal strain ≥15%**	367/382 (96.1)	320/345 (92.8)	—	—
LV mass index <115 g/m^2 for men or <95 g/m^2 for women	319/386 (82.6)	253/351 (72.1)	—	—
LA volume index ≤34 ml/m^2	214/389 (55.0)	161/353 (45.6)	—	—
Change in LV ejection fraction from baseline to 2 years — %††	−1.2±0.4	−1.3±0.4	0.1 (−0.8 to 1.3)	0.66
New-onset atrial fibrillation — no. (%)‡‡	50 (13.0)	48 (12.4)	1.08 (0.73 to 1.60)	—
Death or disabling stroke — no. (%)	44 (9.7)	50 (11.2)	0.87 (0.58 to 1.31)	—
Death	38 (8.4)	41 (9.2)	—	—
Disabling stroke	8 (1.8)	13 (2.9)	—	—

Studie RECOVERY

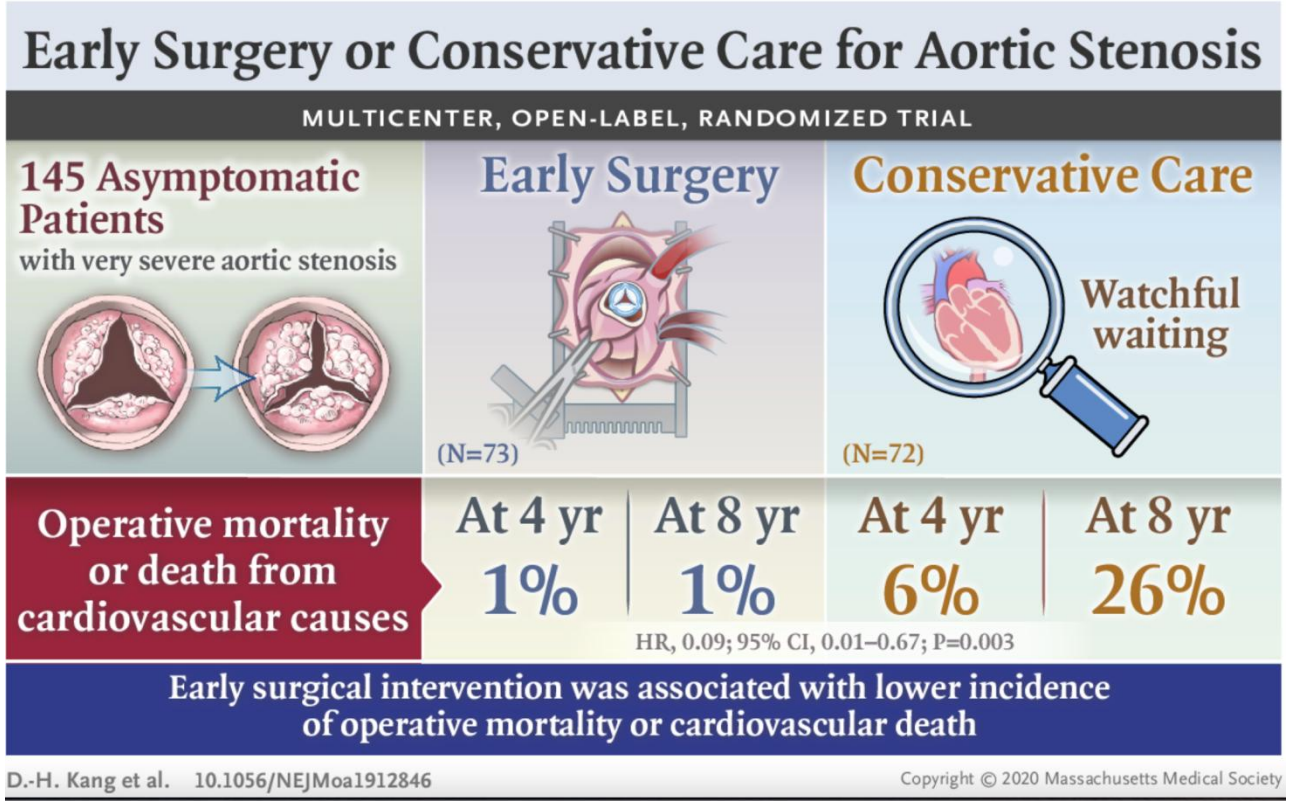


Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Conservative Care (N=72)	Early Surgery (N=73)
Age — yr	63.4±10.7	65.0±7.8
Male sex — no. (%)	34 (47)	37 (51)
Body-surface area — m^2	1.64±0.17	1.69±0.17
Echocardiographic findings		
Cause of aortic stenosis — no. (%)		
Bicuspid aortic valve	39 (54)	49 (67)
Degenerative valvular disease	26 (36)	22 (30)
Rheumatic valvular disease	7 (10)	2 (3)
Peak aortic jet velocity — m/sec	5.04±0.44	5.14±0.52
Transaortic pressure gradient — mm Hg		
Peak	102.5±18.4	106.9±21.9
Mean	62.7±12.4	64.3±14.4
Aortic valve		
Area — cm^2	0.64±0.09	0.63±0.09
Area index — cm^2/m^2	0.39±0.07	0.38±0.06
Left ventricular mass index — g/m^2	133.7±31.1	135.6±38.2
Left ventricular ejection fraction — %	64.8±4.1	64.8±5.2

Symptomatologie pacientů v konzervativní větvi indikovaných k TAVI

	Total	Timing of Conversion to AVR in Months					
		AVR 0 – 6	AVR >6 – 12	AVR >12 – 18	AVR >18 – 24	AVR >24 – 36	AVR >36
Total no. of conversions to AVR — no.	**388**	**116**	**92**	**76**	**28**	**54**	**22**
Patients with Symptoms — no. (%)	**377 (97.2)**	**114 (98.3)**	**89 (96.7)**	**76 (100)**	**28 (100)**	**51 (94.4)**	**19 (86.4)**
Symptom Type — no.							
Dyspnea	313	98	75	57	23	44	16
Angina	94	32	28	13	8	11	2
Dizziness	93	30	25	16	7	13	2
Fatigue	83	21	15	15	9	17	6
Syncope	27	10	7	4	2	2	2
Resuscitated sudden death or cardiac arrest	1	1	0	0	0	0	0
Other†	3	0	1	1	0	1	0
Symptom/HF Severity — no.							
NYHA II	264	78	66	56	17	35	12
NYHA III/IV	113	36	23	20	11	16	7
Hospitalization for HF and/or pulmonary edema — no.	44	13	11	7	7	3	3
≥ 3-fold increase in NT-proBNP‡ — no.	24	2	4	5	2	9	2
Increase in HF medication from baseline — no.	69	16	14	12	8	12	7
Atrial fibrillation — no.	20	2	7	1	4	5	1
LV ejection fraction drops to < 60% — no.	70	22	16	13	7	9	3
LV ejection fraction drops to < 50% — no.	18	5	4	4	2	2	1
Peak velocity > 5 m/s — no.	84	11	26	17	6	14	10
Treatment for other cardiac disease — no.	3	1	0	1	0	1	0
Treatment for non-cardiac disease — no.	4	0	0	1	0	2	1
Ventricular arrhythmia — no.	5	1	0	2	1	0	1

Výskyt u intervenovaných / ze všech v konz. větvi

0.25% / 0.22%

11.3% / 9.8%

6.2% / 5.4%

4.6 % / 4.0%

1.3 % / 1.1%

87% pacientů podstoupilo TAVI a 88% pacientů z nich podstoupilo TAVI do 3 měsíců od vzniku obtíží

Závěry studie EARLY TAVR

- Časná TAVI pacientů s významnou aortální stenózou vede na rozdíl od čekání na symptomy k :
  - Nižšímu nutnosti hospitalizace pro progresi symptomů
  - Lepší kvalitě života
  - Nižšímu výskytu hypertrofie LK a dilataci levé síně
  - Závažné příhody (úmrtí, maligní arytmie, pokles EF LK, plicní edém) byly u obou skupin podobně nízké
  - Zajímavý je vyšší výskyt CMP u pacientů v konz. větvi (9.5% vs. 5.4%, HR 0.62)
- Výsledky platí pro pacienty s průměrným věkem 75 let, normální funkcí LK a pro TAVI za použití chlopně Edwards

Table S7. Procedural Characteristics

	TAVR (N=444)	CS with AVR (N=388)
Type of anesthesia — no. (%)		
General anesthesia	84 (18.9)	73 (18.8)
Conscious sedation	355 (80.0)	311 (80.2)
Conversion from conscious sedation to general anesthesia	5 (1.1)	4 (1.0)
Anesthesia duration — min	117.2 ± 46.1 (444)	119.2 ± 47.1 (386)
Procedure duration — min	40.0 ± 17.7 (443)	45.0 ± 39.4 (380)
Total fluoroscopy time — min†	12.8 ± 6.5 (442)	13.8 ± 6.8 (374)
BAV performed — no./total no. (%)†	125/444 (28.2)	128/381 (33.6)
Final Valve type — no. (%)		
SAPIEN 3	361 (81.3)	215 (55.4)
SAPIEN 3 Ultra	83 (18.7)	156 (40.2)
Surgical valve	---	7 (1.8)
Non-study THV	---	10 (2.6)
Final SAPIEN 3/SAPIEN 3 Ultra size — no. (%)‡		
20 mm	14 (3.2)	3 (0.8)
23 mm	127 (28.6)	129 (34.8)
26 mm	217 (48.9)	170 (45.8)
29 mm	86 (19.4)	69 (18.6)
Post dilatation performed — no./total no. (%)†	62/444 (14.0)	52/380 (13.7)
Cerebral protection device used — no./total no. (%)†	96/444 (21.6)	102/381 (26.8)
More than one THV implanted — no./total no. (%)†	4/444 (0.9)	2/381 (0.5)

Table S8. Periprocedural Safety Outcomes for Patients who Underwent AVR*

	TAVR (N=444)	CS with AVR (N=388)
All cause death	1 (0.2)	0 (0)
Cardiovascular death	0 (0)	0 (0)
Non-cardiovascular death	1 (0.2)	0 (0)
Stroke	4 (0.9)	7 (1.8)
Disabling stroke	0 (0)	4 (1.0)
Non-disabling stroke	4 (0.9)	3 (0.8)
New onset atrial fibrillation†	17 (4.5)	10 (3.1)
Major vascular complications	6 (1.4)	4 (1.0)
Life-threatening/disabling or major bleeding	11 (2.5)	14 (3.6)
Myocardial infarction	2 (0.5)	2 (0.5)
Acute kidney injury‡	11 (2.5)	13 (3.4)
Coronary obstruction requiring intervention	0 (0)	0 (0)
New permanent pacemaker§	24 (5.7)	32 (8.4)