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Transcatheter aortic-valve implantation (TAVI) for aortic stenosis

A systematic review and meta-analysis of randomized clinical trials

2011 - 2 - 22

This report should be referenced as follows:

TrialResults-center.org; Results of all major randomized clinical trials about Transcatheter aortic-valve implantation (TAVI) for aortic stenosis. Accessed at www.trialresultscenter.org/godirect.asp?q=482 on 2011 - 2 - 22

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1 Introduction

1.1 Aim of the report

This report review all the randomized clinical trials of transcatheter aortic-valve implantation (TAVI) for the treatment of aortic stenosis in all type of patients.

1.2 Search strategy

The search aimed to identify all randomized clinical trials relating to the clinical effectiveness of transcatheter aortic-valve implantation (TAVI) for the treatment of aortic stenosis in all type of patients.

1.2.1 Sources searched

The following electronic databases were searched for relevant published literature for the period up to 2011 - 2 - 22:

- MEDLINE,
- EMBASE,
- Cochrane Database of Systematic Reviews (CDSR),
- Cochrane Central Register of Controlled Trials (CCTR),
- Health Technology Assessment (HTA) database,
- ISI Web of Science Proceedings (Index to Scientific and Technical Proceedings),
- ISI Web of Science Science Citation Index Expanded,

Each database was searched as far back as possible, with no language restrictions.

Search strategies of relevant clinical keywords were developed through reference to published strategies, and by iterative searching, whereby keywords identified in references retrieved by initial scoping searches were used to extend the search strategy and so increase the sensitivity of retrieval.

In addition, the reference lists of relevant articles were handsearched.

Attempts to identify further studies were made by consulting health technology assessment and guideline producing agencies, and research and trials registers via the Internet.

Titles and, when available, abstracts of all studies identified in the searches were assessed by a single researcher for relevance to the review. In cases of doubt, the full article was obtained.

1.2.2 Search restrictions

No language, study/publication or date restrictions were applied to the main searches.

1.3 Inclusion criteria

Participants only those studies were included in which the participants had been diagnosed as having established aortic stenosis.

Interventions studies in which transcatheter aortic-valve implantation (TAVI) was used.

Studies using other interventions in addition to transcatheter aortic-valve implantation (TAVI) therapy were included only if the treatment received by the intervention and control groups was identical in all respects other than the use of transcatheter aortic-valve implantation (TAVI).

Methodology randomised controlled trials (RCTs). Trials were accepted as RCTs if the allocation of subjects to treatment groups was described by the authors as either randomised or double-blind.

1.4 Exclusion criteria

Studies considered methodologically unsound. The list of excluded studies with reason of their exclusion are given in a separate section for each treatment categories considered.

1.5 Meta-analysis strategy

Studies that met the reviews entry criteria were eligible for inclusion in the meta-analyses provided that they reported outcomes in terms of the number of subjects suffering clinical outcomes, as only this would allow calculation of the relative risk of subjects in the intervention group developing each outcome, compared with subjects in the control group.

Studies that only presented results in the form of relative risks, relative hazards or odds ratios, without the underlying numbers were also include in the meta-analyses.

Binary outcomes were analysed using the fixed-effect model. For continuous outcomes, weighted mean differences (WMDs) were analysed, using a fixed-effect model.

Heterogeneity was tested by the chi-2 test and the I2 statistic was obtained to describe the proportion of the variability.

Where quantitative heterogeneity was indicated, analysis using a random-effects model was conducted for comparison with results of fixed effect-based analysis. Results of the meta-analysis should be considered as being based on fixed-effect model unless stated otherwise.

Meta-analyses were conducted for data on major stroke, All cause death, stroke or TIA, Death from any cause or major stroke, .

1.6 Structure of the report

Each of the eligible studies is summarised in part I. A summary of the studies together with an evaluation of their quality is given in part ?? to ??, listed by therapeutic class. The therapeutic classes included transcatheter aortic-valve implantation (TAVI),

In these sections, studies in which an active intervention was compared with placebo or no treatment are discussed first, by intervention, followed by a discussion of those studies in which two or more active interventions were compared.

2 Overview of transcatheter aortic-valve implantation (TAVI)1

2.1 Trials

Only one trial which randomized 358 patients was identified. In all, 1 randomized comparison concerned transcatheter aortic valve implantation.

The detailed descriptions of trials and meta-analysis results is given in section 3 (page 13) for transcatheter aortic valve implantation.

This trial included 358 patients and was published in 2010.

This trial was open-label in design.

It was reported in English language.

The table 2.1 (page 10) summarizes the main characteristics of all the included trials. More detailed description is given in the following section.

2.2 Summary of results

The meta-analysis of the available trials about transcatheter aortic-valve implantation (TAVI) provide the results listed in tables 2.2 to 2.2 (page 11) and in the following graphs.

2.2.1 Transcatheter aortic valve implantation

Transcatheter aortic valve implantation was superior to **standard therapy** in terms of death from any cause or major stroke (RR=0.66, 95% CI 0.51 to 0.85, p=0.0000, 1 trial) and all cause death (RR=0.62, 95% CI 0.47 to 0.81, p=0.0000, 1 trial) .But transcatheter aortic valve implantation increased the risk of stroke or TIA (RR=2.38, 95% CI 1.07 to 5.28, p=0.0340, 1 trial) .However, no significant difference was found on major stroke (RR=2.00, 95% CI 0.83 to 4.84, p=0.1240, 1 trial) .

Table 2.1: Main study characteristics - transcatheter aortic-valve implantation (TAVI)

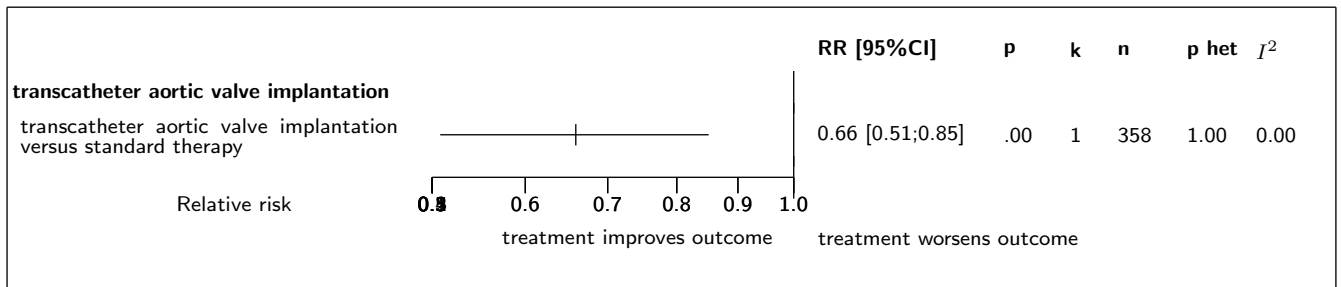
Trial	Patients	Treatments	Trial design and method
Transcatheter aortic valve implantation			
<i>Transcatheter aortic valve implantation versus standard therapy</i>			
PARTNER, 2010 [1] n = 179 vs. 179	patients with severe aortic stenosis considered not to be suitable candidates for surgery	transcatheter aortic-valveimplantation (TAVI)with Edwards SAPIEN Transcatheter Heart Valve versus standard therapy	open parallel groups Primary endpoint: death from any cause 21 centres,USA

Table 2.2: Summary of all results for transcatheter aortic valve implantation

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
<i>transcatheter aortic valve implantation versus standard therapy</i>						
death from any cause or major stroke	RR=0.66	0.51;0.85	0.0000	1.0000 (0.00)	1	358
major stroke	RR=2.00	0.83;4.84	0.1240	1.0000 (0.00)	1	358
stroke or TIA	RR=2.38	1.07;5.28	0.0340	1.0000 (0.00)	1	358
all cause death	RR=0.62	0.47;0.81	0.0000	1.0000 (0.00)	1	358

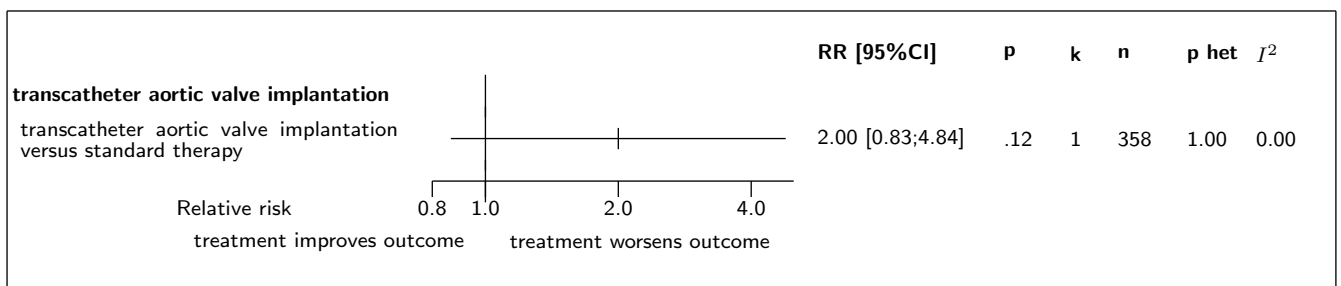
CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Figure 2.1: Forest's plot for death from any cause or major stroke



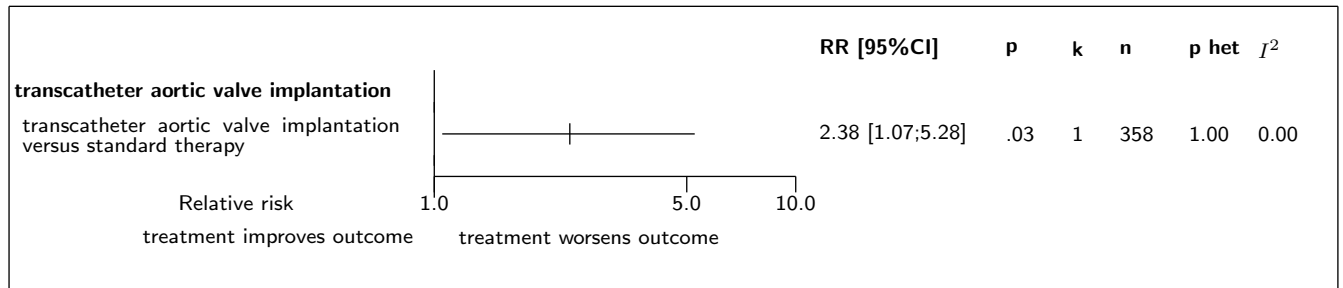
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; ^r: random effect model used

Figure 2.2: Forest's plot for major stroke



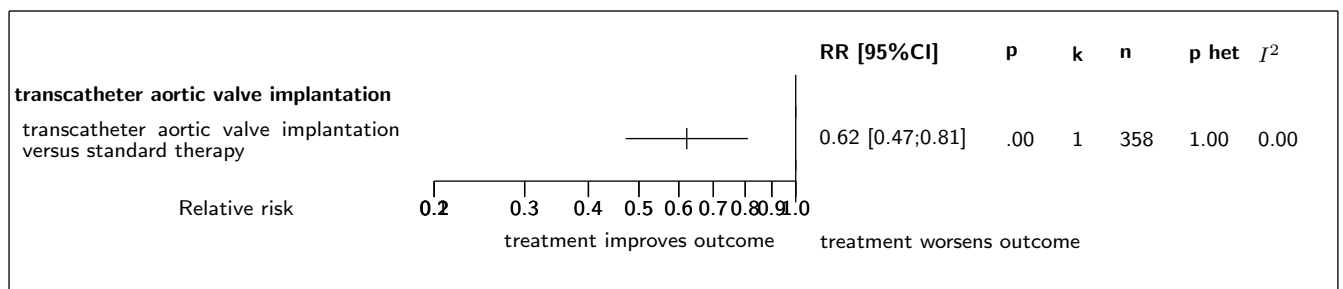
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; ^r: random effect model used

Figure 2.3: Forest's plot for stroke or TIA



Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; ^r: random effect model used

Figure 2.4: Forest's plot for all cause death



Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; ^r: random effect model used

3 Details

3.1 Available trials

Only one trial which randomized 358 patients was identified: it compared transcatheter aortic valve implantation with standard therapy.

This trial included 358 patients and was published in 2010.

This trial was open-label in design.

It was reported in English language.

Major stroke data was reported in 1 trials; 1 trials reported data on all cause death; 1 trials reported data on stroke or TIA; and 1 trials reported data on death from any cause or major stroke.

Following tables 3.1 (page 13), 3.2 (page 13), 3.3 (page 13), and 3.4 (page 14) summarized the main characteristics of the trial including in this systematic review of randomized trials of transcatheter aortic valve implantation.

Table 3.1: *Treatment description - transcatheter aortic-valve implantation (TAVI) - transcatheter aortic valve implantation*

Trial	Studied treatment	Control treatment
Transcatheter aortic valve implantation versus standard therapy		
PARTNER (2010) [1]	transcatheter aortic-valveimplantation (TAVI)with Edwards SAPIEN Transcatheter Heart Valve	standard therapy standard therapy (including balloon aortic-valvuloplasty)

Table 3.2: *Descriptions of participants - transcatheter aortic-valve implantation (TAVI) - transcatheter aortic valve implantation*

Trial	Patients
Transcatheter aortic valve implantation versus standard therapy	
PARTNER (2010) [1]	Patients with severe aortic stenosis considerednot to be suitable candidates for surgery

Table 3.3: *Main patients characteristics - transcatheter aortic-valve implantation (TAVI) - transcatheter aortic valve implantation*

Trial	Characteristics
Transcatheter aortic valve implantation versus standard therapy	
PARTNER, 2010 [1]	

Table 3.4: Design and methodological quality of trials - transcatheter aortic-valve implantation (TAVI) - transcatheter aortic valve implantation

Trial	Design	Duration	Centre	Primary end-point
Transcatheter aortic valve implantation versus standard therapy				
PARTNER, 2010 [1] n=358	Parallel groups open confirmatory trial at risk of bias	1.6 y (at least 1 year) inclusion period: may 2007 - Mar 2009	USA 21 centres	death from any cause

3.2 Meta-analysis results

The results are detailed in table 3.5 (page 14). This table is followed by the Forest's plot corresponding to each endpoint.

Transcatheter aortic valve implantation versus standard therapy

The single study eligible for this comparison provided data on **death from any cause or major stroke**. The analysis detected a statistically significant difference in favor of transcatheter aortic valve implantation in death from any cause or major stroke, with a RR of 0.66 (95% CI 0.51 to 0.85, $p=0.0000$).

The single study eligible for this comparison provided data on **major stroke**. No statistically significant difference between the groups was found in major stroke, with a RR of 2.00 (95% CI 0.83 to 4.84, $p=0.1240$).

The single study eligible for this comparison provided data on **stroke or TIA**. The analysis detected a statistically significant difference in favor of standard therapy in stroke or TIA, with a RR of 2.38 (95% CI 1.07 to 5.28, $p=0.0340$).

The single study eligible for this comparison provided data on **all cause death**. The analysis detected a statistically significant difference in favor of transcatheter aortic valve implantation in all cause death, with a RR of 0.62 (95% CI 0.47 to 0.81, $p=0.0000$).

Table 3.5: Results details - transcatheter aortic-valve implantation (TAVI) - transcatheter aortic valve implantation

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
transcatheter aortic valve implantation versus standard therapy						
death from any cause or major stroke	RR=0.66	[0.51;0.85]	0.0000	1.0000 ($I^2=0.00$)	1	358
major stroke	RR=2.00	[0.83;4.84]	0.1240	1.0000 ($I^2=0.00$)	1	358
stroke or TIA	RR=2.38	[1.07;5.28]	0.0340	1.0000 ($I^2=0.00$)	1	358
all cause death	RR=0.62	[0.47;0.81]	0.0000	1.0000 ($I^2=0.00$)	1	358

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2 : inconsistency degree

Figure 3.1: Forest's plot for death from any cause or major stroke

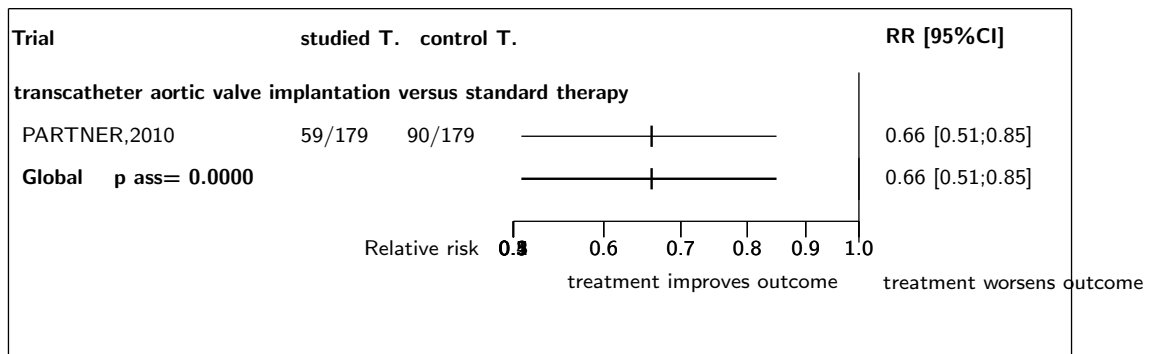


Figure 3.2: Forest's plot for major stroke

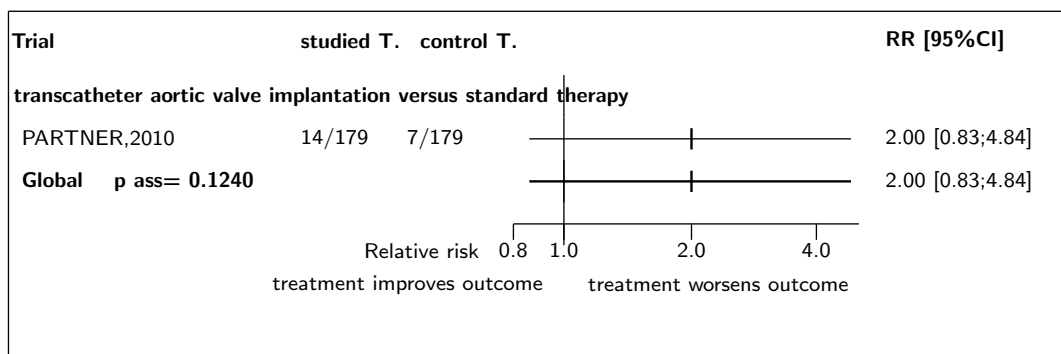


Figure 3.3: Forest's plot for stroke or TIA

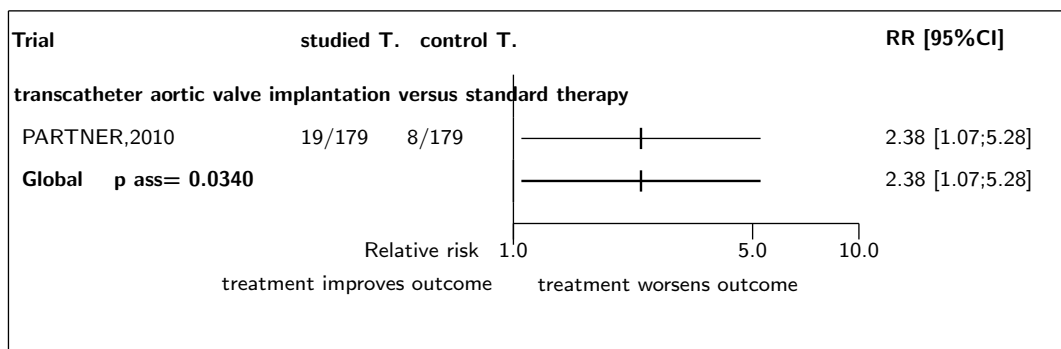
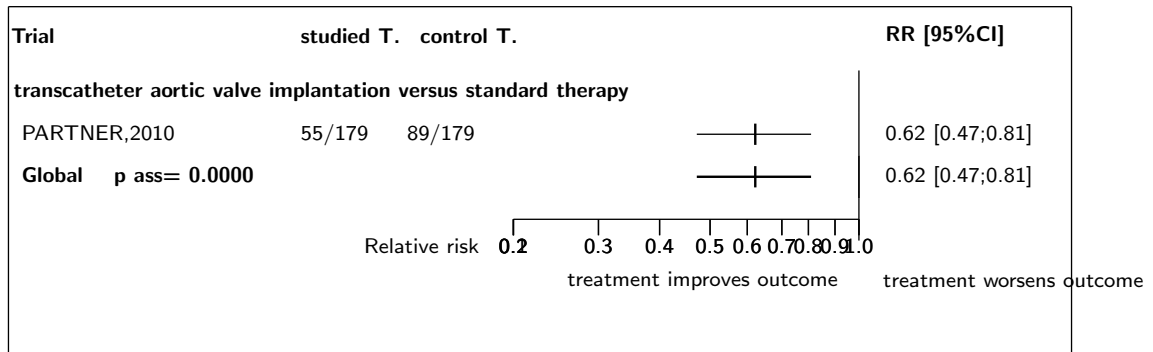


Figure 3.4: Forest’s plot for all cause death



References

- [1] Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010 Oct 21;363:1597-607. [PMID=20961243]

4 Global meta-analysis: all transcatheter aortic-valve implantation (TAVI)

4.1 Global meta-analysis: all transcatheter aortic-valve implantation (TAVI) versus standard therapy

Table 4.1: All transcatheter aortic-valve implantation (TAVI) versus standard therapy

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n	Plot
death from any cause or major stroke	RR=0.66	0.51;0.85	0.0000	1.0000 (0.00)	1	358	_____
major stroke	RR=2.00	0.83;4.84	0.1240	1.0000 (0.00)	1	358	_____
stroke or TIA	RR=2.38	1.07;5.28	0.0340	1.0000 (0.00)	1	358	_____
all cause death	RR=0.62	0.47;0.81	0.0000	1.0000 (0.00)	1	358	_____

legend B

5 Ongoing studies

A total of 2 ongoing studies were still ongoing at the date of this report. A list of these ongoing studies with a brief description is given table 5.1.

Table 5.1: *Ongoing studies for transcatheter aortic-valve implantation (TAVI)*

Study	Description
CoreValve US pivotal trial NCT01240902	percutaneous valve implantation (Surgical Valve Replacement) vs. conventional aortic-valve surgery High Risk and Very High Risk Subjects Who Need Aortic Valve Replacement
PARTNER cohort A NCT00530894	percutaneous valve implantation (Sapien device) vs. Surgical Valve Replacement high risk, symptomatic patients with severe aortic stenosis

6 Excluded studies

No trial was excluded.

Part I

Trial's summary - Evidence table

Table 6.1: PARTNER, 2010 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
n=358 (179 vs. 179)	Patients with severe aortic stenosis considered not to be suitable candidates for surgery	Studied treatment: transcatheter aortic-valveimplantation (TAVI)with Edwards SAPIEN Transcatheter Heart Valve Control treatment: standard therapy standard therapy (including balloon aorticvalvuloplasty)	Death from any cause or major stroke RR=0.66 [0.51;0.85] Major stroke RR=2.00 [0.83;4.84] Stroke or TIA RR=2.38 [1.07;5.28] All cause death RR=0.62 [0.47;0.81]
Follow-up duration: 1.6 y (at least 1 year)			
Study design: Randomized controlled trial Parallel groups Open			
Confirmatory trial at risk of bias			
USA, 21 centres			
Inclusion period: may 2007 - Mar 2009			
Reference			
Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010 Oct 21;363:1597-607 [PMID=20961243]			

