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Dr. Fernando Ribeiro de Moraes Neto
Dr. Luciano Cabral Albuquerque
Dr. Orlando Petrucci Junior
Dr. Walter José Gomes

SOCIEDADE
BRASILEIRA DE
CIRURGIA
CARDIOVASCULAR

EDITORIAL

EXCEL Trial – As controvérsias e as soluções em vista

O estudo EXCEL[1] foi um estudo randomizado de não inferioridade, desenvolvido para comparar cirurgia de revascularização do miocárdio (CRM) e intervenção coronária percutânea (ICP) em pacientes com lesão de tronco de artéria coronária esquerda (LT) com escore SYNTAX < 32. Evidências anteriores, derivadas do estudo SYNTAX[2], mostraram definitivamente os benefícios do tratamento cirúrgico em pacientes com LT de alto risco (escore SYNTAX > 32), com recomendação classe I; no entanto, pacientes com escore SYNTAX < 32 (risco baixo e intermediário) poderiam ter resultados semelhantes em longo prazo, com qualquer uma das intervenções. Como o estudo SYNTAX não foi estatisticamente desenvolvido para resolver esse problema, foram necessários mais estudos, como o EXCEL.

A publicação dos resultados de 5 anos do estudo EXCEL na revista New England Journal of Medicine revelou na conclusão não ter havido diferença significativa entre ICP e CRM, em relação às taxas do desfecho composto de morte, acidente vascular cerebral ou infarto do miocárdio (IM) , entre pacientes com LT e complexidade anatômica baixa ou intermediária (conforme definido pelo escore SYNTAX).

Entretanto, quando da sua publicação, sérias preocupações sobre transgressões éticas e científicas com o estudo EXCEL foram levantadas.

O desfecho isolado de morte por qualquer causa favoreceu significativamente a CRM aos 5 anos (9,9% vs. 13% com ICP; OR 1,38; IC 95% 1,03-1,85) e, observando-se o gráfico de sobrevida, claramente as curvas de sobrevivência continuam divergindo ao longo do tempo, favorecendo a terapia cirúrgica. De fato, a taxa de mortalidade em 5 anos foi 38% maior no grupo da ICP do que no grupo da CRM.

A conclusão do estudo EXCEL foi possível apenas porque a definição de infarto do miocárdio (IM) periprocedimento foi modificada com o estudo já em andamento, em inequívoco desvio de protocolo, favorecendo a ICP. Os pesquisadores do estudo EXCEL passaram a utilizar a definição de IM da Sociedade de Angiografia e Intervenções Cardiovasculares, em vez da Definição Universal de Infarto do Miocárdio, que havia sido previamente registrada no protocolo original. Essa decisão, introduzida posteriormente durante a fase de coleta de dados, determinou um efeito crucial, criando uma taxa 37% maior de IM periprocedimento no grupo da CRM, alterando, portanto, o resultado final.

A consequência de deixar este artigo da maneira com esta redação é que induzirá cardiologistas, cirurgiões e pacientes em todo o mundo a decisões clínicas errôneas, pois esses resultados serão incluídos em diretrizes, podendo aumentar o número de pacientes encaminhados para uma forma de tratamento, que se mostrou inferior.

A implicação dessa atitude será potencialmente prejudicial também para os sistemas de saúde, pública ou privada, que precisarão custear procedimentos desnecessários e talvez prejudiciais.

Várias organizações científicas importantes em todo o mundo demandaram maior transparência, requerendo uma revisão independente dos dados brutos do estudo EXCEL, por revisores externos neutros e imparciais, em relação à questão crítica do conflito de interesses.

Ademais, com o objetivo de restaurar a credibilidade em nossa profissão e proteger nossos pacientes, há de se estabelecer limites à prática de introduzir vieses em estudos clínicos. Socie-

dades de profissionais médicos, agências reguladoras e sistemas de saúde nacionais ou internacionais devem unir forças e trabalhar juntos em projetos de desenvolvimento e publicação de estudos importantes e decisivos, permitindo a produção de dados transparentes, honestos e criveis. A Sociedade Brasileira de Cirurgia Cardiovascular publicou esta semana uma análise crítica e fundamentada em evidências, sob forma de Editorial, no European Journal of Cardiothoracic Surgery, em 15 de maio de 2020[3], em que profundamente são discutidas todas as falhas metodológicas, que trazem tamanhas incertezas aos resultados do estudo EXCEL, a ponto de ter requerida sua retirada das citações do último Guidelines da ESC, para revascularização miocárdica. Recomendamos a leitura na íntegra.

Walter José Gomes, Luciano Albuquerque

REFERÊNCIAS

1. Stone GW, Kappetein AP, Sabik JF, Pocock SJ, Morice MC, Puskas J et al. Five-year outcomes after PCI or CABG for left main coronary disease. N Engl J Med 2019;381:1820–30.
2. Mohr FW, Morice M-C, Kappetein AP, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. Lancet 2013; 381: 629–38.
3. Gomes WJ, Albuquerque LC, Jatene FB, Leal JC, Rocha EA, Almeida RM, on behalf of the Brazilian Society of Cardiovascular Surgery. The transfiguration of the EXCEL trial: exceeding ethical and moral boundaries. Eur J Cardiothorac Surg, may 15, doi:10.1093/ejcts/ezaa121.

N Engl J Med 2020;382:1395-1407

ISCHEMIA Trial: em pacientes com doença coronariana estável, a estratégia invasiva de investigação/intervenção não demonstrou benefício, em relação ao tratamento clínico

Initial Invasive or Conservative Strategy for Stable Coronary Disease

BACKGROUND

Among patients with stable coronary disease and moderate or severe ischemia, whether clinical outcomes are better in those who receive an invasive intervention plus medical therapy than in those who receive medical therapy alone is uncertain.

METHODS

We randomly assigned 5179 patients with moderate or severe ischemia to an initial invasive strategy (angiography and revascularization when feasible) and medical therapy or to an initial conservative strategy of medical therapy alone and angiography if medical therapy failed. The primary outcome was a composite of death from cardiovascular causes, myocardial infarction, or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest. A key secondary outcome was death from cardiovascular causes or myocardial infarction.

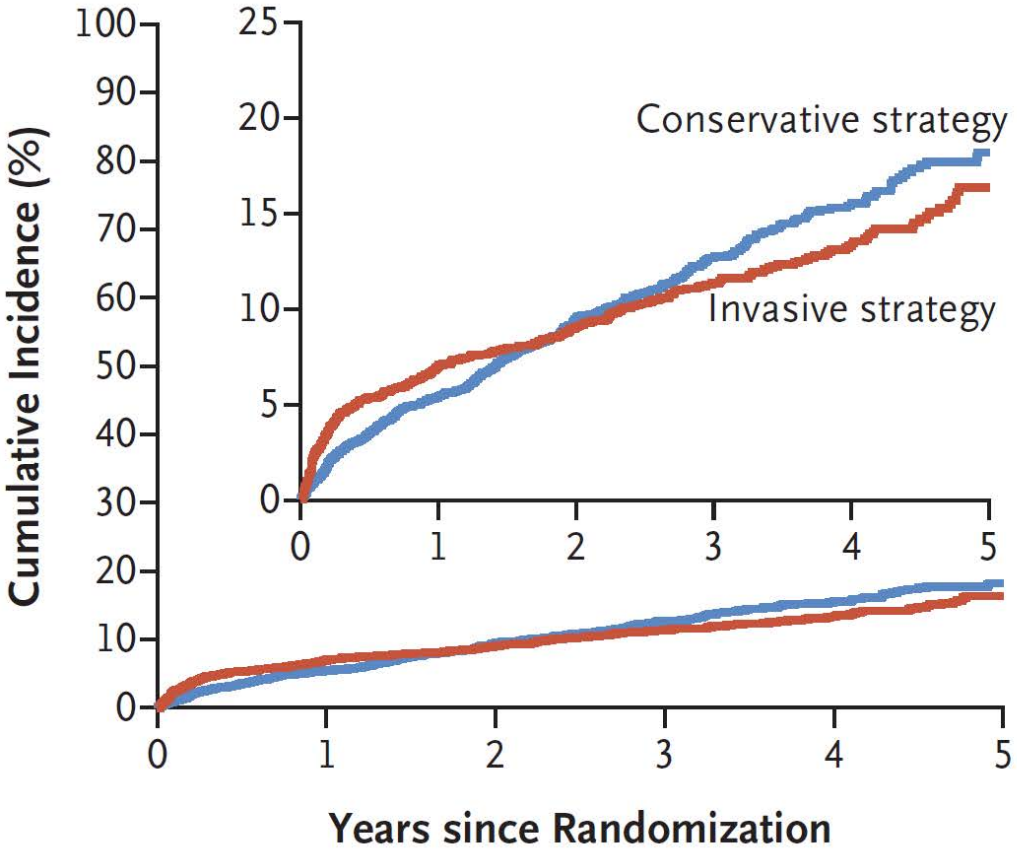
RESULTS

Over a median of 3.2 years, 318 primary outcome events occurred in the invasive-strategy group and 352 occurred in the conservative-strategy group. At 6 months, the cumulative event rate was 5.3% in the invasive-strategy group and 3.4% in the conservative-strategy group (difference, 1.9 percentage points; 95% confidence interval [CI], 0.8 to 3.0); at 5 years, the cumulative event rate was 16.4% and 18.2%, respectively (difference, -1.8 percentage points; 95% CI, -4.7 to 1.0). Results were similar with respect to the key secondary outcome. The incidence of the primary outcome was sensitive to the definition of myocardial infarction; a secondary analysis yielded more procedural myocardial infarctions of uncertain clinical importance. There were 145 deaths in the invasive-strategy group and 144 deaths in the conservative-strategy group (hazard ratio, 1.05; 95% CI, 0.83 to 1.32).

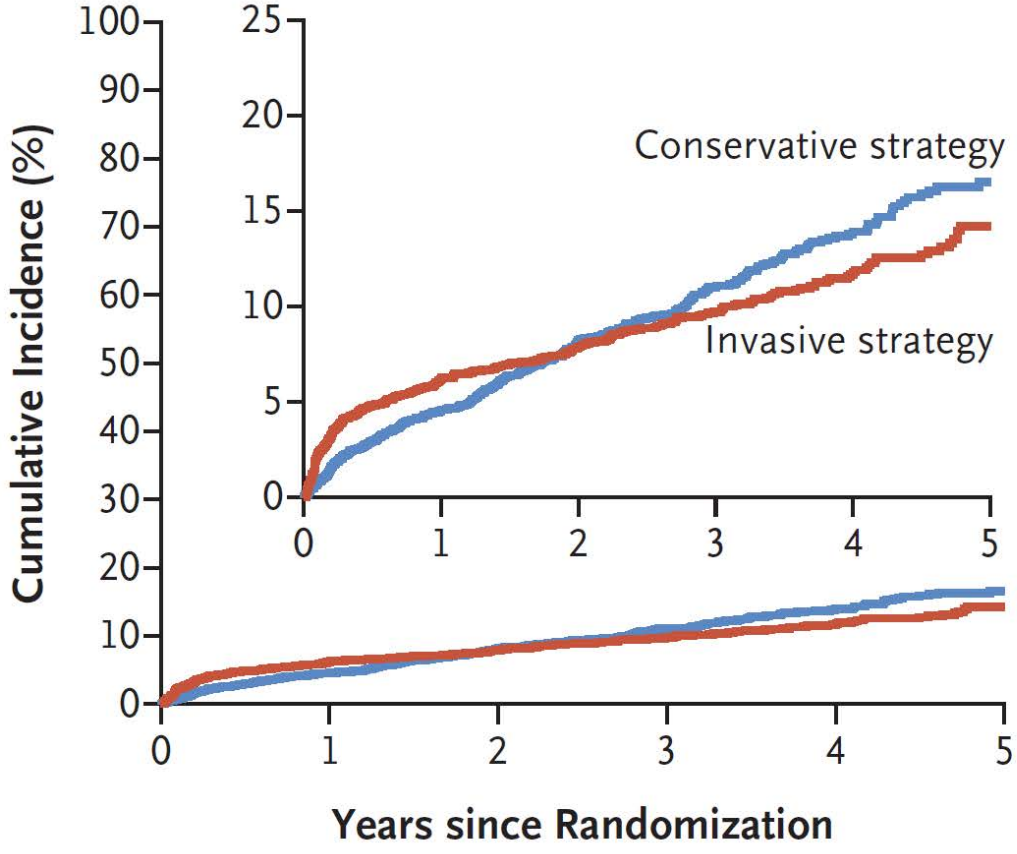
CONCLUSIONS

Among patients with stable coronary disease and moderate or severe ischemia, we did not find evidence that an initial invasive strategy, as compared with an initial conservative strategy, reduced the risk of ischemic cardiovascular events or death from any cause over a median of 3.2 years. The trial findings were sensitive to the definition of myocardial infarction that was used. (Funded by the National Heart, Lung, and Blood Institute and others; ISCHEMIA ClinicalTrials.gov number, NCT01471522.).

A Primary Composite Outcome



B Death from Cardiovascular Causes or Myocardial Infarction



PARTNER 3 Trial: em pacientes com estenose aórtica e baixo risco cirúrgico, o implante de TAVI apresentou melhores resultados em 1 ano, do que a cirurgia convencional

Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

BACKGROUND

Among patients with aortic stenosis who are at intermediate or high risk for death with surgery, major outcomes are similar with transcatheter aortic-valve replacement (TAVR) and surgical aortic-valve replacement. There is insufficient evidence regarding the comparison of the two procedures in patients who are at low risk.

METHODS

We randomly assigned patients with severe aortic stenosis and low surgical risk to undergo either TAVR with transfemoral placement of a balloon-expandable valve or surgery. The primary end point was a composite of death, stroke, or rehospitalization at 1 year. Both noninferiority testing (with a prespecified margin of 6 percentage points) and superiority testing were performed in the as-treated population.

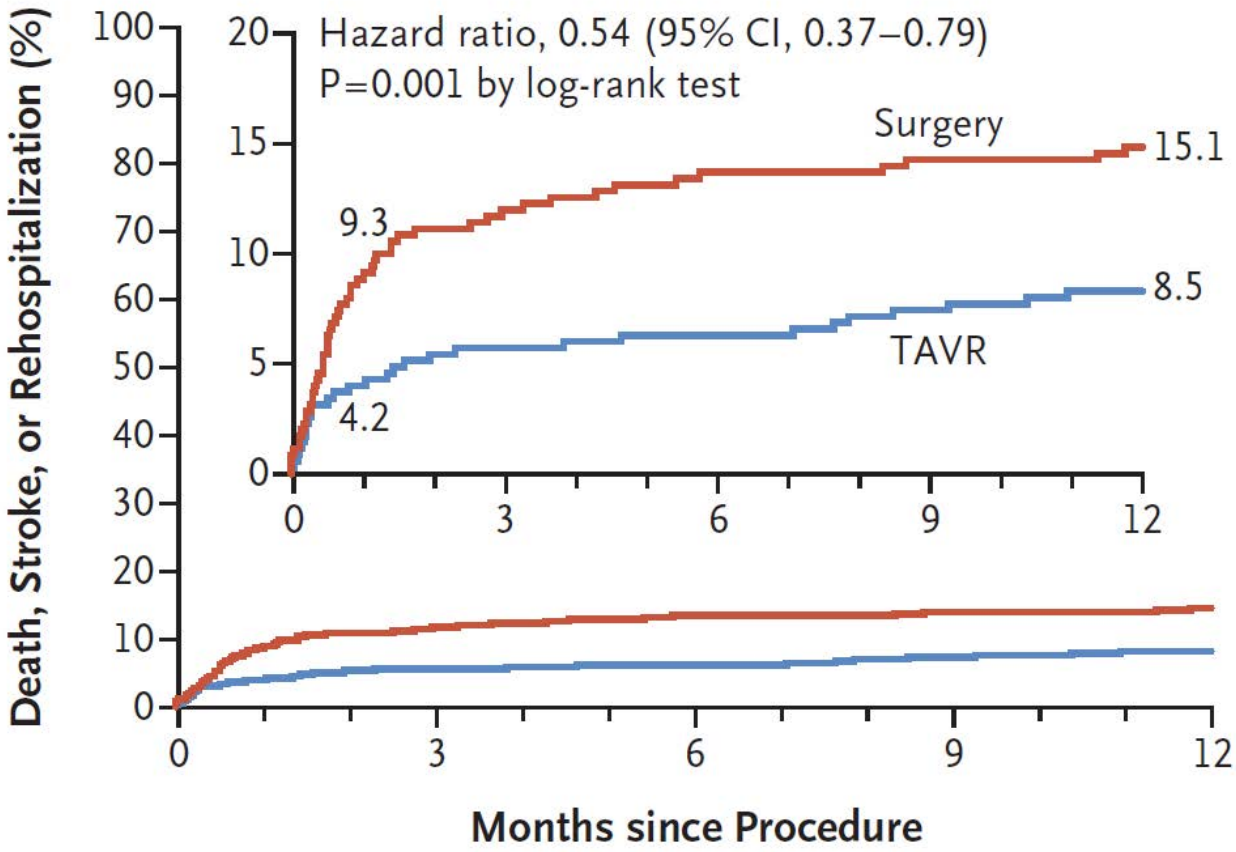
RESULTS

At 71 centers, 1000 patients underwent randomization. The mean age of the patients was 73 years, and the mean Society of Thoracic Surgeons risk score was 1.9% (with scores ranging from 0 to 100% and higher scores indicating a greater risk of death within 30 days after the procedure). The Kaplan-Meier estimate of the rate of the primary composite end point at 1 year was significantly lower in the TAVR group than in the surgery group (8.5% *vs.* 15.1%; absolute difference, -6.6 percentage points; 95% confidence interval [CI], -10.8 to -2.5; $P<0.001$ for noninferiority; hazard ratio, 0.54; 95% CI, 0.37 to 0.79; $P=0.001$ for superiority). At 30 days, TAVR resulted in a lower rate of stroke than surgery ($P=0.02$) and in lower rates of death or stroke ($P=0.01$) and new-onset atrial fibrillation ($P<0.001$). TAVR also resulted in a shorter index hospitalization than surgery ($P<0.001$) and in a lower risk of a poor treatment outcome (death or a low Kansas City Cardiomyopathy Questionnaire score) at 30 days ($P<0.001$). There were no significant between-group differences in major vascular complications, new permanent pacemaker insertions, or moderate or severe paravalvular regurgitation.

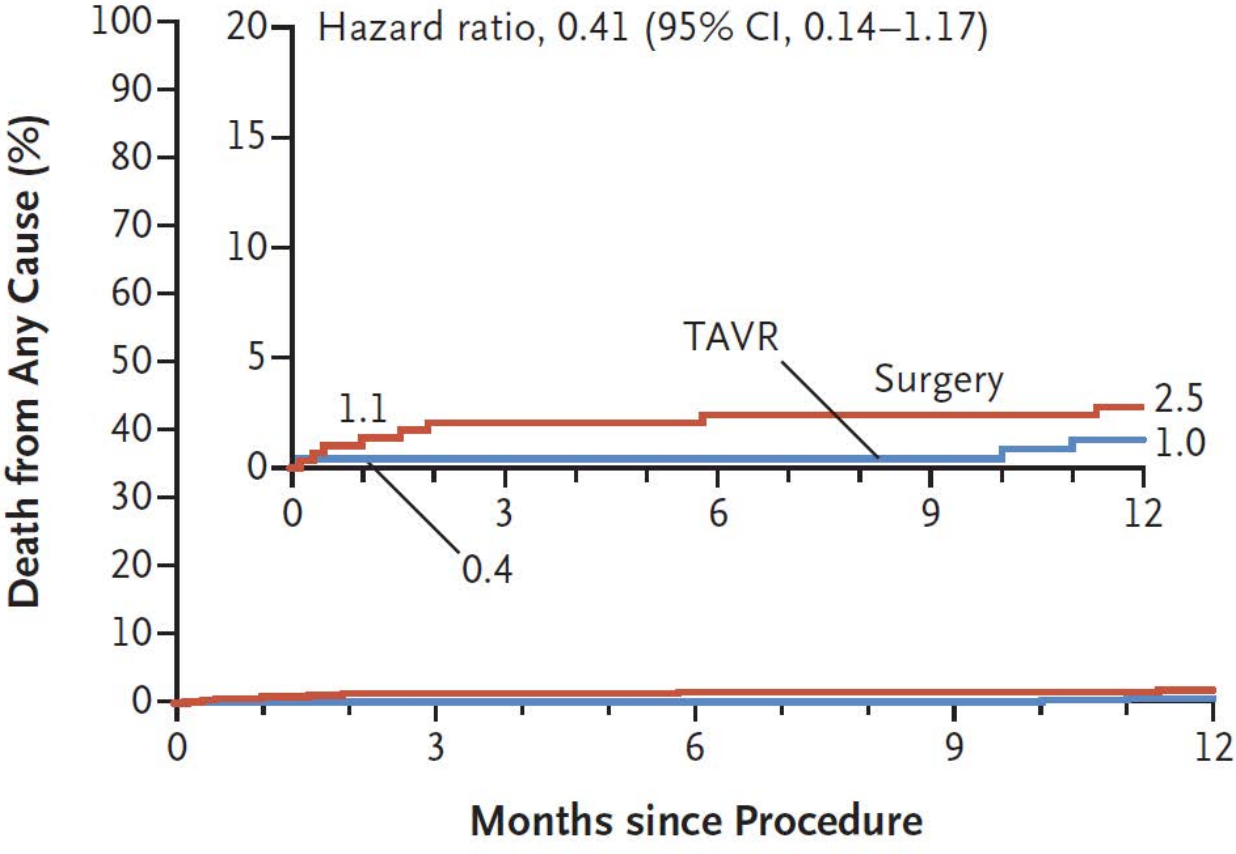
CONCLUSIONS

Among patients with severe aortic stenosis who were at low surgical risk, the rate of the composite of death, stroke, or rehospitalization at 1 year was significantly lower with TAVR than with surgery. (Funded by Edwards Lifesciences; PARTNER 3 ClinicalTrials.gov number, NCT02675114).

A


Death, Stroke, or Rehospitalization (%)
Hazard ratio, 0.54 (95% CI, 0.37–0.79)
P=0.001 by log-rank test
Surgery
TAVR
9.3
15.1
8.5
4.2
Months since Procedure

B


Death from Any Cause (%)
Hazard ratio, 0.41 (95% CI, 0.14–1.17)
TAVR
Surgery
1.1
2.5
1.0
0.4
Months since Procedure

Estudo multicêntrico avalia resultados de reimplante transcateter de válvula aórtica (TAVI-in--TAVI)

Repeat Transcatheter Aortic Valve Replacement for Transcatheter Prosthesis Dysfunction

BACKGROUND

Transcatheter aortic valve replacement (TAVR) use is increasing in patients with longer life expectancy, yet robust data on the durability of transcatheter heart valves (THVs) are limited. Redo-TAVR may play a key strategy in treating patients in whom THVs fail.

OBJECTIVES

The authors sought to examine outcomes following redo-TAVR.

METHODS

The Redo-TAVR registry collected data on consecutive patients who underwent redo--TAVR at 37 centers. Patients were classified as probable TAVR failure or probable THV failure if they presented within or beyond 1 year of their index TAVR, respectively.

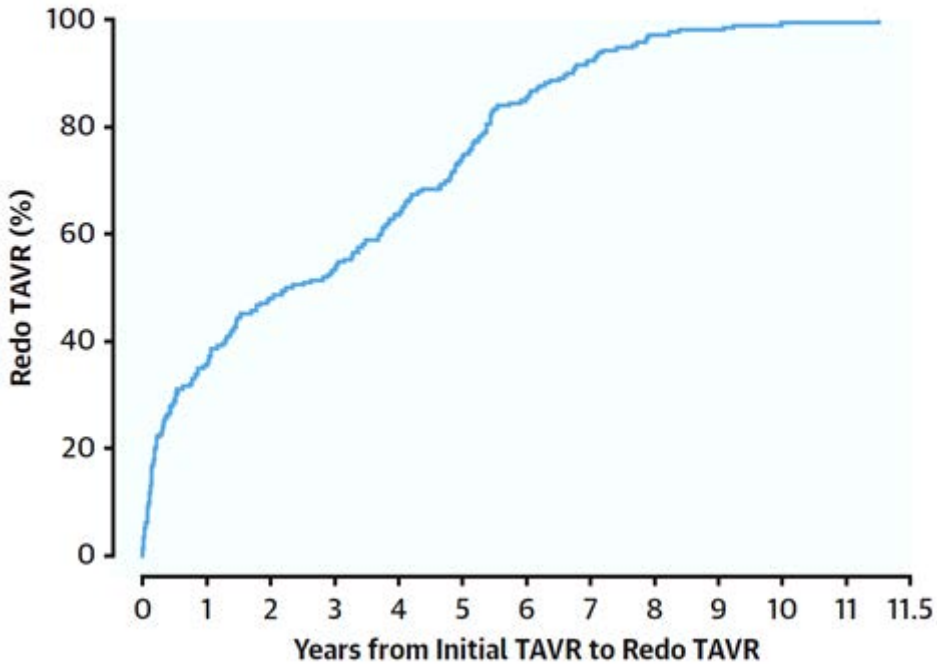
RESULTS

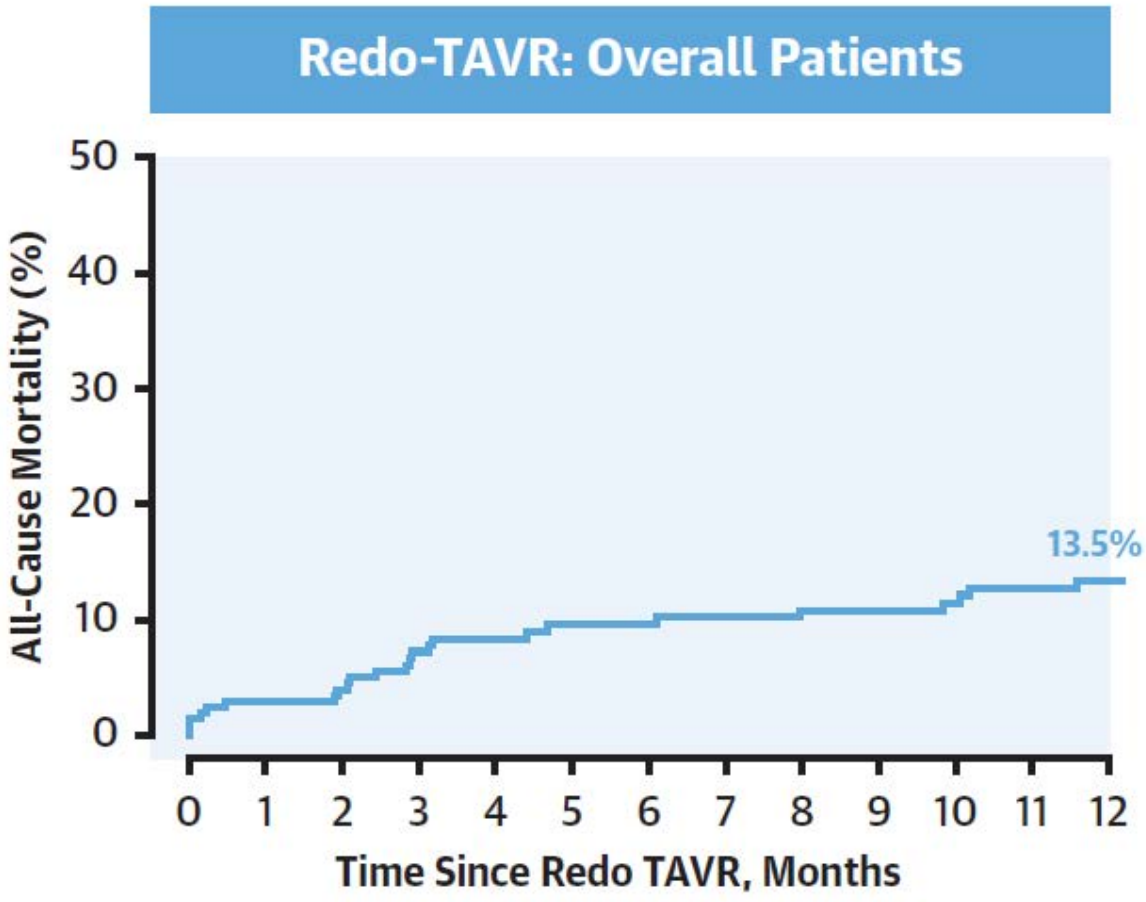
Among 63,876 TAVR procedures, 212 consecutive redo-TAVR procedures were identified (0.33%): 74 within and 138 beyond 1 year of the initial procedure. For these 2 groups, TAVR-to-redo-TAVR time was 68 (38 to 154) days and 5 (3 to 6) years. The indication for redo--TAVR was THV stenosis in 12 (16.2%) and 51 (37.0%) (*P*=0.002) and regurgitation or combined stenosis-regurgitation in 62 (83.8%) and 86 (62.3%) (*P*=0.028), respectively. Device success using VARC-2 criteria was achieved in 180 patients (85.1%); most failures were attributable to high residual gradients (14.1%) or regurgitation (8.9%). At 30-day and 1-year follow-up, residual gradients were 12.6±7.5 mm Hg and 12.9±9.0 mm Hg; valve area 1.63±0.61 cm2 and 1.51±0.57 cm2; and regurgitation ⩽mild in 91% and 91%, respectively. Peri-procedural complication rates were low (3 stroke [1.4%], 7 valve malposition [3.3%], 2 coronary obstruction [0.9%], 20 new permanent pacemaker [9.6%], no mortality), and symptomatic improvement was substantial. Survival at 30 days was 94.6% and 98.5% (*P*=0.101) and 83.6% and 88.3% (*P*=0.335) at 1 year for patients presenting with early and late valve dysfunction, respectively.

CONCLUSIONS

Redo-TAVR is a relatively safe and effective option for selected patients with valve dysfunction after TAVR. These results are important for applicability of TAVR in patients with long life expectancy in whom THV durability may be a concern.

First TAVI to Redo-TAVI Time Interval Distribuition





Neurology 2020;94:876-85

Academia Americana de Neurologia atualiza recomendações para a prevenção de AVC, em pacientes com forâmen oval patente (FOP)

Practice Advisory Update Summary: Patent Foramen Ovale and Secondary Stroke Prevention: Report of the Guideline Subcommittee of the American Academy of Neurology

OBJECTIVE

To update the 2016 American Academy of Neurology (AAN) practice advisory for patients with stroke and patent foramen ovale (PFO).

METHODS

The guideline panel followed the AAN 2017 guideline development process to systematically review studies published through December 2017 and formulate recommendations.

MAJOR RECOMMENDATIONS

In patients being considered for PFO closure, clinicians should ensure that an appropriately thorough evaluation has been performed to rule out alternative mechanisms of stroke (level B). In patients with a higher risk alternative mechanism of stroke identified, clinicians should not routinely recommend PFO closure (level B). Clinicians should counsel patients that having a PFO is common; that it occurs in about 1 in 4 adults in the general population; that it is difficult to determine with certainty whether their PFO caused their stroke; and that PFO closure probably reduces recurrent stroke risk in select patients (level B). In patients younger than 60 years with a PFO and embolic-appearing infarct and no other mechanism of stroke identified, clinicians may recommend closure following a discussion of potential benefits (absolute recurrent stroke risk reduction of 3.4% at 5 years) and risks (periprocedural complication rate of 3.9% and increased absolute rate of non-periprocedural atrial fibrillation of 0.33% per year) (level C). In patients who opt to receive medical therapy alone without PFO closure, clinicians may recommend an antiplatelet medication such as aspirin or anticoagulation (level C).

Ann Thorac Surg 2020;109:1467-74

Resultados tardios da fenestração na Operação de Fontan: Uma Meta-análise e Revisão

Effect of Fenestration on Fontan Procedure Outcomes: A Meta-Analysis and Review

BACKGROUND

Many studies investigating fenestration in the context of Fontan procedure have been showing controversial results when it comes to whether this procedure truly improves the Surgical outcomes. The aim of this meta-analysis was to compare the early outcomes of a fenestrated (F) vs a nonfenestrated (NF) Fontan procedure.

METHODS

The PubMed, EMBASE, and Cochrane Library databases were searched for articles measuring the outcomes of an F vs an NF Fontan.

RESULTS

A total of 19 studies were selected with a total of 4806 patients (F. 2727; NF. 2079). There was no difference in the risk of Fontan failure between both groups (odds ratio [OR], 0.95 [95% confidence interval [CI], 0.57, 1.56]; *P*=.83). The F group had a significantly lower need for pleural drainage (OR, 0.59 [95% CI, 0.37, 0.94]; *P*=.03), a lower pulmonary artery pressure (mean difference, -0.99 mm Hg [95% CI, -1.68, 0.30 mm Hg]; *P*=.005), and a lower oxygen saturation (mean difference, -3.07% [95% CI, -4.30%, -1.85%]; *P*<.001) than the NF group. There was no significant difference in the stroke occurrence between the 2 groups (OR, 1.32 [95% CI, 0.40, 4.36]; *P*=.65).

CONCLUSIONS

The Fontan fenestration effectively reduced the pulmonary pressure and the need for prolonged pleural drainage. However, the risks of Fontan failure, early death, and longer hospital stay were not modified.