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SYNTAXES Study: Seguimento de 10 anos do SYNTAX Trial Mantém Benefício da CRM em Pacientes Multiarteriais e em Lesões Anatomicamente Complexas (Syntax score ≥ 33)

Percutaneous Coronary Intervention versus Coronary Artery Bypass Grafting in Patients with Three-Vessel or Left Main Coronary Artery Disease: 10-year Follow-Up of the Multicentre Randomised Controlled SYNTAX Trial

BACKGROUND

The Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial was a non-inferiority trial that compared percutaneous coronary intervention (PCI) using first-generation paclitaxel-eluting stents with coronary artery bypass grafting (CABG) in patients with de-novo three-vessel and left main coronary artery disease, and reported results up to 5 years. We now report 10-year all-cause death results.

METHODS

The SYNTAX Extended Survival (SYNTAXES) study is an investigator-driven extension of follow-up of a multicentre, randomised controlled trial done in 85 hospitals across 18 North American and European countries. Patients with de-novo three-vessel and left main coronary artery disease were randomly assigned (1:1) to the PCI group or CABG group. Patients with a history of PCI or CABG, acute myocardial infarction, or an indication for concomitant cardiac surgery were excluded. The primary endpoint of the SYNTAXES study was 10-year all-cause death, which was assessed according to the intention-to-treat principle. Prespecified subgroup analyses were performed according to the presence or absence of left main coronary artery disease and diabetes, and according to coronary complexity defined by core laboratory SYNTAX score tertiles. This study is registered with ClinicalTrials.gov, NCT03417050.

FINDINGS

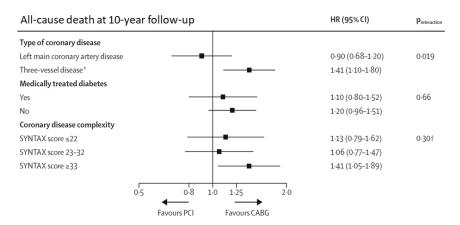
From March, 2005, to April, 2007, 1800 patients were randomly assigned to the PCI (n=903) or CABG (n=897) group. Vital status information at 10 years was complete for 841 (93%) patients in the PCI group and 848 (95%) patients in the CABG group. At 10 years, 244 (27%) patients had died after PCI and 211 (24%) after CABG (hazard ratio 1.17)

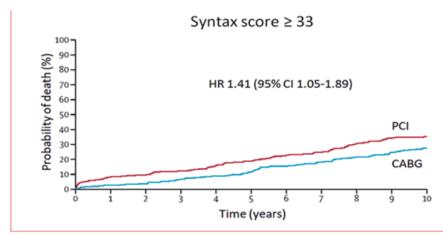


[95% CI 0.97–1.41], P=0.092). Among patients with three vessel disease, 151 (28%) of 546 had died after PCI versus 113 (21%) of 549 after CABG (hazard ratio 1.41 [95% CI 1.10–1.80]), and among patients with left main coronary artery disease, 93 (26%) of 357 had died after PCI versus 98 (28%) of 348 after CABG (0.90 [0.68–1.20], pinteraction=0.019). There was no treatment-by-subgroup interaction with diabetes (pinteraction=0.66) and no linear trend across SYNTAX score tertiles (ptrend=0.30).

INTERPRETATION

At 10 years, no significant difference existed in all-cause death between PCI using first-generation paclitaxel-eluting stents and CABG. However, CABG provided a significant survival benefit in patients with three-vessel disease, but not in patients with left main coronary artery disease.





Implications of all the available evidence

Patients with complex, three-vessel coronary artery disease who require revascularisation should undergo CABG as it results in significantly lower all-cause death than PCI. In selected patients with left main coronary artery disease, PCI is a suitable alternative to CABG and provides similar 10-year survival.



Subanálise do Estudo EXCEL Aponta Maior Mortalidade nos Pacientes Operados Sem Circulação Extracorpórea

Off-Pump versus On-Pump Bypass Surgery for Left Main Coronary Artery Disease

BACKGROUND

Concerns remain for a greater risk of incomplete revascularization and reduced survival with off-pumpcoronary artery bypass grafting (CABG) surgery compared with on-pump surgery particularly in patients with left maindisease and extensive underlying myocardial ischemia.

OBJECTIVES

This study sought to compare outcomes following off-pump versus on-pump surgery for left main diseaseby performing a post hoc analysis from the multicenter, randomized EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial.

METHODS

The EXCEL trial was designed to compare percutaneous coronary intervention with everolimus-elutingstents versus CABG in patients with left main disease. CABG was performed with or without cardiopulmonary bypass (on-pump vs. off-pump surgery) according to the discretion of the operator. The 3-year outcomes in the off-pump and on-pump groups were compared using inverse probability of treatment weighting (IPTW) for treatment effect estimation.

RESULTS

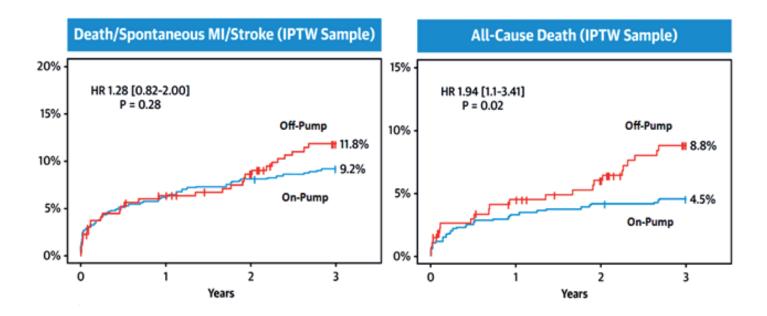
Among 923 CABG patients, 652 and 271 patients underwent onpump and off-pump surgery, respectively. Despite a similar extent of disease, off-pump surgery was associated with a lower rate of revascularization of the left circumflex coronary artery (84.1% vs. 90.0%; p $\frac{1}{4}$ 0.01) and right coronary artery (31.1% vs. 40.6%; p $\frac{1}{4}$ 0.007). After IPTW adjustment for baseline differences, off-pump surgery was associated with a significantly increased risk of 3-year all-cause death (8.8% vs. 4.5%; hazard ratio: 1.94; 95% confidence interval: 1.10 to 3.41; p $\frac{1}{4}$ 0.02) and a nonsignificant difference in the risk for the composite endpoint



of death, myocardial infarction, or stroke (11.8% vs. 9.2%; hazard ratio: 1.28; 95% confidence interval: 0.82 to 2.00; p $\frac{1}{4}$ 0.28).

CONCLUSIONS

Among patients with left main disease treated with CABG in the EXCEL trial, off-pump surgery was associated with a lower rate of revascularization of the coronary arteries supplying the inferolateral wall and an increased risk of 3-year all-cause death compared with onpump surgery.





Avaliação da Importância da Viabilidade Miocárdica na Revascularização de Pacientes Com Disfunção Ventricular Grave: seguimento de 10 anos do Estudo STICH

Myocardial Viability and Long-Term Outcomes in Ischemic Cardiomyopathy

BACKGROUND

The role of assessment of myocardial viability in identifying patients with ischemic cardiomyopathy who might benefit from surgical revascularization remains controversial. Furthermore, although improvement in left ventricular function is one of the goals of revascularization, its relationship to subsequent outcomes is unclear.

METHODS

Among 601 patients who had coronary artery disease that was amenable to coronaryartery bypass grafting (CABG) and who had a left ventricular ejection fraction of 35% or lower, we prospectively assessed myocardial viability using single-photonemission computed tomography, dobutamine echocardiography, or both. Patients were randomly assigned to undergo CABG and receive medical therapy or to receive medical therapy alone. Left ventricular ejection fraction was measured at baseline and after 4 months of follow-up in 318 patients. The primary end point was death from any cause. The median duration of follow-up was 10.4 years.

RESULTS

CABG plus medical therapy was associated with a lower incidence of death from any cause than medical therapy alone (182 deaths among 298 patients in the CABG group vs. 209 deaths among 303 patients in the medical-therapy group; adjusted hazard ratio, 0.73; 95% confidence interval, 0.60 to 0.90). However, no significant interaction was observed between the presence or absence of myocardial viability and the beneficial effect of CABG plus medical therapy over medical therapy alone (P=0.34 for interaction). An increase in left ventricular ejection fraction was observed only among patients with myocardial

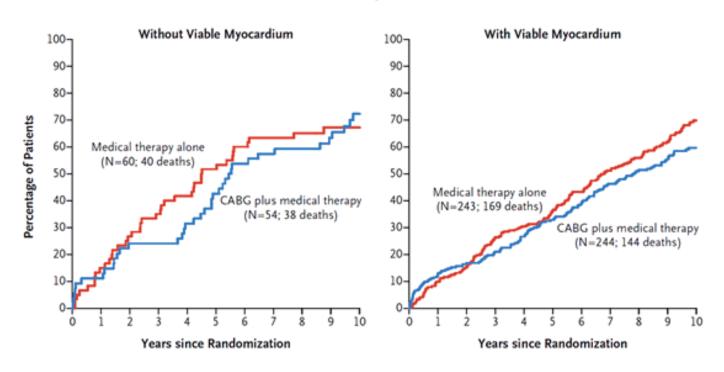


viability, irrespective of treatments signment. There was no association between changes in left ventricular ejection fraction and subsequent death.

CONCLUSIONS

The findings of this study do not support the concept that myocardial viability is associated with a long-term benefit of CABG in patients with ischemic cardiomyopathy. The presence of viable myocardium was associated with improvement in left ventricular systolic function, irrespective of treatment, but such improvement was not related to long-term survival.

Death from Any Cause, According to Myocardial Viability Status





COMENTÁRIO EDITORIAL

O STICH trial representa um dos mais importantes estudos doença coronária, e o único ensaio clínico testanto o papel da revascularização miocárdica, em pacientes com disfunção grave de ventrículo esquerdo. Entretanto, os resultados dos braços do estudo que avaliaram a importância da restauração ventricular e da documentação de viabilidade miocárdica, têm sido alvo de ampla discussão e controvérsia, ao longo da última década.

Estes resultados de 10 anos do subgrupo do STICH trial que avaliou viabilidade miocárdica, reafirma a incapacidade de relacionar-se a comprovação de viabilidade ao aumento de sobrevida, nos pacientes submetidos a CRM. Não obstante esses achados, é importante lembrar as sérias limitações e viéses de seleção e de métodos de imagem utilizados, reconhecidos em diversos Editorias, alguns assinados por seus próprios autores1,2,3 : (1) menos de 50% dos pacientes alocados ao STICH trial realizaram estudo de viabilidade (n=601); (2) a seleção dos pacientes submetidos a pesquisa de viabilidade ocorreu de forma não randomizada; (3) o critério de viabilidade foi estabelecido de forma binária (presença ou ausência), sem ter havido quantificação da área de isquemia ou de necrose: e (4) foram utilizados apenas dois métodos de imagem, o ecocardiograma com dobutamina e a tomografia com emissão de fóton único (SPECT), de acordo com a escolha do centro, não tendo sido utilizados exames mais acurados, como a tomografia com emissão de pósitrons (PET) e a ressonância magnética.

Talvez por estas razões, a conclusão do STICH viabilidade esteja em paradoxal confronto ao conceito fisiopatológico de que, ao se revascularizar células miocárdicas vivas, espera-se um resultado melhor do que o contrário.

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Luciano Cabral Albuquerque



REGROUP Trial: Retirada Convencional e Endoscópica de Veia Safena, Apresentam Desfechos Semelhantes, em Pacientes Submetidos a Revascularização Miocárdica

Randomized Trial of Endoscopic or Open Vein- Graft Harvesting for Coronary-Artery Bypass

BACKGROUND

The saphenous-vein graft is the most common conduit for coronary-artery bypass grafting (CABG). The influence of the vein-graft harvesting technique on long term clinical outcomes has not been well characterized.

METHODS

We randomly assigned patients undergoing CABG at 16 Veterans Affairs cardiac surgery centers to either open or endoscopic vein-graft harvesting. The primary outcome was a composite of major adverse cardiac events, including death from any cause, nonfatal myocardial infarction, and repeat revascularization. Leg-wound complications were also evaluated.

RESULTS

A total of 1150 patients underwent randomization. Over a median follow-up of 2.78 years, the primary outcome occurred in 89 patients (15.5%) in the open harvest group and 80 patients (13.9%) in the endoscopic-harvest group (hazard ratio, 1.12; 95% confidence interval [CI], 0.83 to 1.51; P=0.47). A total of 46 patients (8.0%) in the open-harvest group and 37 patients (6.4%) in the endoscopic harvest group died (hazard ratio, 1.25; 95% CI, 0.81 to 1.92); myocardial infarctions occurred in 34 patients (5.9%) in the open-harvest group and 27 patients (4.7%) in the endoscopic-harvest group (hazard ratio, 1.27; 95% CI, 0.77 to 2.11), and revascularization occurred in 35 patients (6.1%) in the open-harvest group and 31 patients (5.4%) in the endoscopic-harvest group (hazard ratio, 1.14; 95% CI, 0.70 to 1.85). Leg-wound infections occurred in 18 patients (3.1%) in the open-harvest group and in 8 patients (1.4%) in the endoscopic-harvest group (relative risk, 2.26; 95% CI, 0.99 to 5.15).



CONCLUSIONS

Among patients undergoing CABG, we did not find a significant difference between open vein-graft harvesting and endoscopic veingraft harvesting in the risk of major adverse cardiac events.

Event	Open Harvesting (N = 574)	Endoscopic Harvesting (N = 576)	Hazard Ratio (95% CI)
	number of patients (percent)		
Primary outcome: death from any cause, nonfatal myocardial infarction, or repeat revascularization	89 (15.5)	80 (13.9)	1.12 (0.83–1.51)*
Death from any cause	46 (8.0)	37 (6.4)	1.25 (0.81-1.92)
Myocardial infarction	34 (5.9)	27 (4.7)	1.27 (0.77-2.11)
Repeat revascularization	35 (6.1)	31 (5.4)	1.14 (0.70-1.85)

NORTION Trial Demonstra Não Inferioridade da Válvula Aórtica Transcateter (TAVI) em Comparação à Troca Valvar, em Pacientes de Baixo Risco

Five-Year Clinical and Echocardiographic Outcomes from the Nordic Aortic Valve Intervention (NOTION) Randomized Clinical Trial in Lower Surgical Risk Patients

BACKGROUND

The Nordic Aortic Valve Intervention (NOTION) was designed to compare transcatheter aortic valve replacement (TAVR) to surgical aortic valve replacement (SAVR) in patients 70 years or older with isolated severe aortic valve stenosis. Clinical and echocardiographic outcomes are presented after 5 years.

METHODS

Patients were enrolled at three Nordic centers and randomized 1:1 to TAVR using the self-expanding CoreValve prosthesis (n=145) or SAVR using any stented bio-prostheses (n=135). The primary composite outcome was the rate of all-cause mortality, stroke, or myocardial infarction at 1 year defined according to Valve Academic Research Consortium-2 criteria.

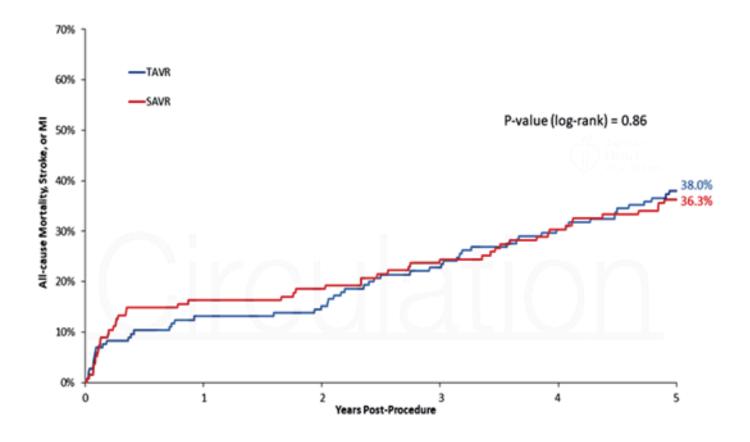
RESULTS

Baseline characteristics were similar. The mean age was 79.1±4.8 years and mean STS-PROM score was 3.0%±1.7%. After 5 years, there were no differences between TAVR and SAVR in the composite outcome (Kaplan-Meier estimates 38.0% vs. 36.3%, log-rank test P=0.86) or any of its components. TAVR patients had larger prosthetic valve area (1.7 cm2 vs. 1.2 cm2, P<0.001) with a lower mean transprosthetic gradient (8.2 mm Hg vs. 13.7 mm Hg, P<0.001), both unchanged over time. More TAVR patients had moderate/severe total aortic regurgitation (8.2% vs. 0.0%, P<0.001) and a new pacemaker (43.7% vs. 8.7%, P<0.001). Four patients had prosthetic re-interventionand no difference was found for functional outcomes.



CONCLUSIONS

These are currently the longest follow-up data comparing TAVR and SAVR in lower risk patients, demonstrating no statistical difference for major clinical outcomes 5 years after TAVR with a self-expanding prosthesis compared to SAVR. Higher rates of prosthetic regurgitation and pacemaker implantation were seen after TAVR.





https://www.ctsnet.org/jans/fda-expands-indication-several-transcatheter-heart-valves-patients-low-risk

FDA Aprova Válvula Aórtica Transcateter (TAVI) em Pacientes de Baixo Risco

FDA Expands Indication for Several Transcatheter Heart Valves to Patients at Low Risk

The U.S. Food and Drug Administration to day approved an expanded indication for several transcatheter heart valves to include patients with severe aortic valve stenosis (a narrowing of the heart's aortic valve that restricts blood flow to aorta, the body's main artery) who are at low risk for death or major complications associated with open-heart surgery to replace the damaged valves. These transcatheter valves - Sapien 3, Sapien 3 Ultra, CoreValve Evolut R and CoreValve Evolut PRO - were previously indicated only for patients at intermediate or higher risk for death or major complications during open-heart surgery. In low risk patients, open-heart surgery has been the standard-of-care for aortic valve replacement. However, the procedure to insert a transcatheter heart valve is less invasive, and involves a smaller incision and shorter recovery time than open-heart surgery. The FDA is the first medical products regulatory body in the world to expand the indication for these devices to patients at low risk for death or major complications associated with open-heart surgery.

As part of the approval of these devices, the FDA is requiring each manufacturer to continue to follow patients enrolled in their randomized studies for 10 years to further monitor transcatheter aortic valve safety and effectiveness, including the long-term valve durability. The manufacturers will also participate in the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry to provide FDA with additional surveillance of these devices over a 10-year period.

The approval of the Sapien 3 and Sapien 3 Ultra was granted to Edwards Lifesciences LLC. The approval of the CoreValve Evolut R and CoreValve Evolut PRO was granted to Medtronic CoreValve LLC.



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RevisãoSistemáticaApontaMaisAltaIncidênciadePlaquetopenia Pós-Operatória nas Válvulas Aórticas Transcateter, de Liberação Rápida e Stentless, em Comparação à Prótese Convencional

Peri-Procedural Thrombocytopenia after Aortic Bioprosthesis Implant: A Systematic Review and Meta-Analysis Comparison Among Conventional, Stentless, Rapid-Deployment, and Transcatheter Valves

BACKGROUND

Thrombocytopenia has been shown to occur soon after surgical biological aortic valve replacement (AVR), and recently reported also aftertranscathetervalveimplantation (TAVI). The mechanism underlying this phenomenon is still unknown, and its clinical impact on the perioperative outcome has been poorly investigated.

METHODS

A systematic review and a meta-analysis of all available studies reporting data about peri-procedural thrombocytopenia on isolated bio-AVR, comparing rapid-deployment (RDV), stentless (sAVR), and TAVI vs. stented (SAVR) valves, have been performed.

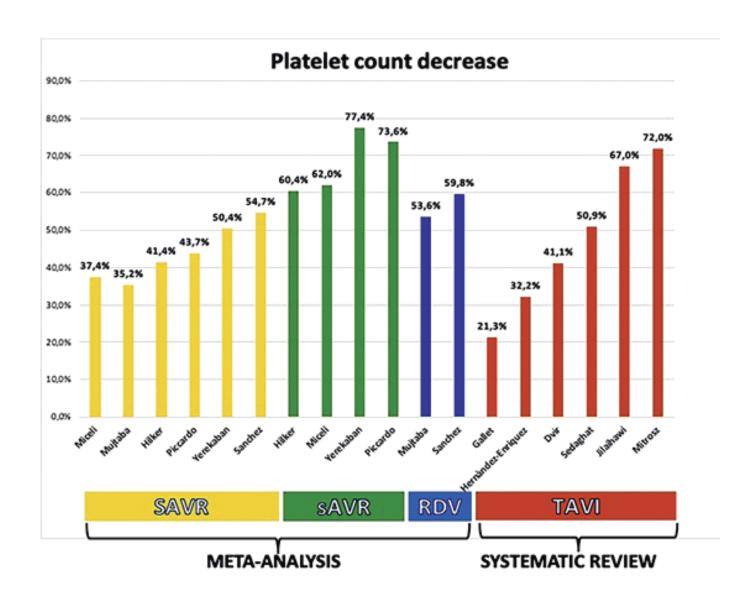
RESULTS

Fifteen trials (2.163 patients)were included in the meta-analysis. Perioperative platelet reduction ranged from 35% to 55% in stented-AVR, from 60% to 77% in stentless-AVR, from 53% to 60% in RDV, and from to 21% to 72% in TAVI (apparently, balloon-expandable valves more frequently associated to thrombocytopenia). Stented- AVR required more red blood cells transfusion than stentless-AVR (P b 0.0001), whereas no difference has been found between RDV and stented-AVR. Platelet transfusion rate was very low in all surgical groups. No difference has been found in RDV and stentless-AVR vs. stented-AVR, in terms of reoperation for bleeding, and length-ofintensive care unit or hospital stay.



CONCLUSIONS

Thrombocytopenia-related major adverse events were mainly reported in TAVI patients, whereas clinically meaningless in surgical patients. Transient peri-procedural thrombocytopenia is common after bio-AVR, regardless of prosthesis's type or implant modality. It should receive appropriate monitoring and focused investigations.





COMENTÁRIO EDITORIAL

Plaquetopenia após Procedimentos Valvares Aórticos

A plaquetopenia tem sido um evento reconhecido como de ocorrência eventual após a cirurgia de troca valvar aórtica, seja com prótese mecânica ou biológica. Entretanto, suas consequências são consideradas de curta duração, sem repercussões clínicas e totalmente reversíveis. Mas com uma nova geração de próteses valvares chegando à prática médica atual, as evidências de achados de plaquetopenia nestes dispositivos indicam que esta relação pode afetar adversamente os resultados pós-operatórios.

Na meta-análise de Jiritano e cols, comparando a ocorrência de plaquetonia peri-procedimento entre troca valvar aórtica convencional, próteses de implante rápido, stentlesse TAVI (implante de válvula aórtica transcateter), no grupo das próteses implantadas cirurgicamente, as válvulas de implante rápido e as stentless apresentaram maior incidência de plaquetopenia pós-operatória em comparação com o grupo de troca aórtica convencional. Entretanto, nestes grupos, a ocorrência da plaquetonia não esteve associada ao aumento da morbimortalidade, sendo um evento transitório que reverteu entre 10 a 15 dias sem tratamento específico.

Por outro lado, a incidência de plaquetopenia com a TAVI variou de 25% a 100% e foi associada independentemente ao aumento de mortalidade hospitalar (P=0,002). A plaquetopenia pós-operatória persistente após TAVI foi descrita em até 35% dos pacientes, e uma queda na contagem de plaquetas >30% após a TAVI foi associada a maiores taxas de sangramentos e óbitos em 30 dias, quando comparados a uma queda ≤30%.

As próteses expansíveis por balão parecem provocar maior plaquetopenia que as próteses autoexpansíveis, com um estudo observacional relatando maior mortalidade cardíaca no grupo que utilizou prótese expansível por balão em comparação à prótese autoexpansível após 5 anos de acompanhamento.

Várias hipóteses têm sido levantadas para explicar essa associação, mas acredita-se que seja multifatorial. É aparente que o mecanismo envolve vários componentes, associados ao tipo de dispositivo, ao procedimento e fatores relacionados ao paciente.

No entanto, nesse campo há ainda uma escassez de dados de boa qualidade e esses resultados devem ser interpretado com cautela,



devido à natureza observacional da maioria desses estudos e com limitação por amostras pequenas. A confirmação desses dados em coortes maiores de pacientes e estudos bem conduzidos se fazem necessários.

Walter José Gomes

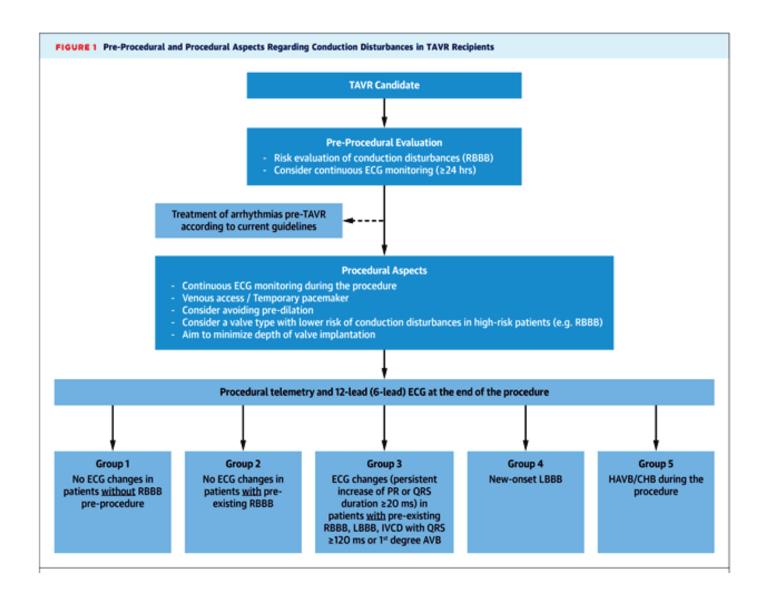


Consenso de Especialistas Aborda Manejo das Arritmias Associadas ao Implante de Válvula Aórtica Transcateter (TAVI)

Management of Conduction Disturbances Associated with Transcatheter Aortic Valve Replacement: JACC Scientific Expert Panel

Despite major improvements in transcatheter aortic valve replacement (TAVR) periprocedural complications in recent years, the occurrence of conduction disturbances has not decreased over time and remains the most frequent complication of the procedure. Additionally, there has been an important lack of consensus on the management of these complications, which has indeed translated into a high degree of uncertainty regarding the most appropriate treatment of a large proportion of such patients along with major differences between centers and studies in pacemaker rates post-TAVR. There is therefore an urgent need for a uniform strategy regarding the management of conduction disturbances after TAVR. The present expert consensus scientific panel document has been formulated by a multidisciplinary group of interventional cardiologists, electrophysiologists, and cardiac surgeons as an initial attempt to provide a guide for the management of conduction disturbances after TAVR based on the best available data and group expertise.







Metanálise Aponta Piores Desfechos com o Tratamento Endovascular, em Comparação à Cirurgia Convencional, na Correção Eletiva de Aneurisma da Aorta Abdominal (AAA)

A Systematic Review and Meta-Analysis of the Long-Term Outcomes of Endovascular versus Open Repair of Abdominal Aortic Aneurysm

OBJECTIVE

This study synthesized the literature comparing the long-term (5-9 years) and very long-term (≥10 years) all-cause mortality, reintervention, and secondary rupture rates between endovascular aneurysm repair (EVAR) and open surgical repair (OSR) of abdominal aortic aneurysm (AAA).

METHODS

MEDLINE, Embase, and CENTRAL databases were searched from inception to May 2018 for studies comparing EVAR to OSR with a minimum follow-up period of 5 years. Study selection, data abstraction, and quality assessment were conducted by two independent reviewers, with a third author resolving discrepancies. Study quality was assessed using the Cochrane and Newcastle-Ottawa scales. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using random-effects models. Heterogeneity was quantified using the I2 statistic, and publication bias was assessed using funnel plots.

RESULTS

Our search yielded 3431 unique articles. Three randomized controlled trials and 68 observational studies comparing 151,092 EVAR to 148,692 OSR patients were included. Inter-rater agreement was excellent at the screening (κ = 0.78) and full-text review (κ = 0.89) stages. Overall, the risk of bias was low to moderate. For long-term outcomes, 54 studies reported all-cause mortality (n=203,246), 23 reported reintervention (n=157,151), and 4 reported secondary rupture (n=150,135). EVAR was associated with higher long-term all-cause mortality (OR, 1.19; 95% CI, 1.06-1.33; P=.003, I2 = 91%), reintervention (OR, 2.12; 95% CI, 1.67-2.69; P<.00001, I2 = 96%), and secondary rupture rates (OR, 4.84; 95% CI,



2.63-8.89; P<.00001, I2 = 92%). For very long-term outcomes, 15 studies reported all-cause mortality (n=48,721), 9 reported reintervention (n=7511), and 1 reported secondary rupture (n=1116). There was no mortality difference between groups, but EVAR was associated with higher reintervention (OR, 2.47; 95% CI, 1.71-3.57; P<.00001, I2 = 84%) and secondary rupture rates (OR, 8.10; 95% CI, 1.01-64.99; P=.05). Subanalysis of more recent studies, with last year of patient recruitment 2010 or after, demonstrated no long-term mortality differences between EVAR and OSR.

CONCLUSIONS

EVAR is associated with higher long-term all-cause mortality, reintervention, and secondary rupture rates compared with OSR. In the very long-term, EVAR is also associated with higher reintervention and secondary rupture rates. Notably, EVAR mortality has improved over time. Vigilant long-term surveillance of EVAR patients is recommended.



Associação entre crescimento e desenvolvimento cerebral com a idade da correção de transposição das grandes artérias, com a técnica de Switch Operation

Associations Between Age at Arterial Switch Operation, Brain Growth, and Development in Infants With Transposition of the Great Arteries

BACKGROUND

Brain injury, impaired brain growth, and long-term neurodevelopmental problems are common in children with transposition of the great arteries. We sought to identify clinical risk factors for brain injury and poor brain growth in infants with transposition of the great arteries undergoing the arterial switch operation, and to examine their relationship with neurodevelopmental outcome.

METHODS

The brains of 45 infants with transposition of the great arteries undergoing surgical repair were imaged pre- and postoperatively using magnetic resonance imaging. Brain weight z scores were calculated based on brain volume and autopsy reference data. Brain injury scores were determined as previously described. Neurodevelopment was assessed at 18 months using the Bayley-III scores of infantdevelopment. The relationships between clinical variables, brain injury, perioperative brain growth, and 18-month Bayley-III scores were analyzed.

RESULTS

On preoperative imaging, moderate or severe white matter injury was present in 10 of 45 patients, whereas stroke was seen in 4 of 45. A similar prevalence of injury was seen on postoperative imaging, and we were unable to identify any clinical risk factors for braininjury. Brain weight z scores decreased perioperatively in 35 of 45 patients. The presence of a ventricular septal defect (P=0.009) and older age at surgery (P=0.007) were associated with impaired perioperative brain growth. When patients were divided into those undergoing surgery during the first 2 weeks of life (32/45) versus those being repaired later



(13/45), infants repaired later had significantly worse perioperative brain growth (late repair postoperative brain weight $z = -1.0\pm0.90$ versus early repair $z = -0.33\pm0.64$; P=0.008). Bayley-III testing scores fell within the normal range for all patients, although age at repair (P=0.03) and days of open chest (P=0.03) were associated with a lower composite language score, and length of stay was associated with a lower composite cognitive score (P=0.02).

CONCLUSIONS

Surgery beyond 2 weeks of age is associated with impaired brain growth and slower language development in infants with transposition of the great arteries cared for at our center. Although the mechanisms underlying this association are still unclear, extended periods of cyanosis and pulmonary overcirculation may adversely impact brain growth and subsequent neurodevelopment.

