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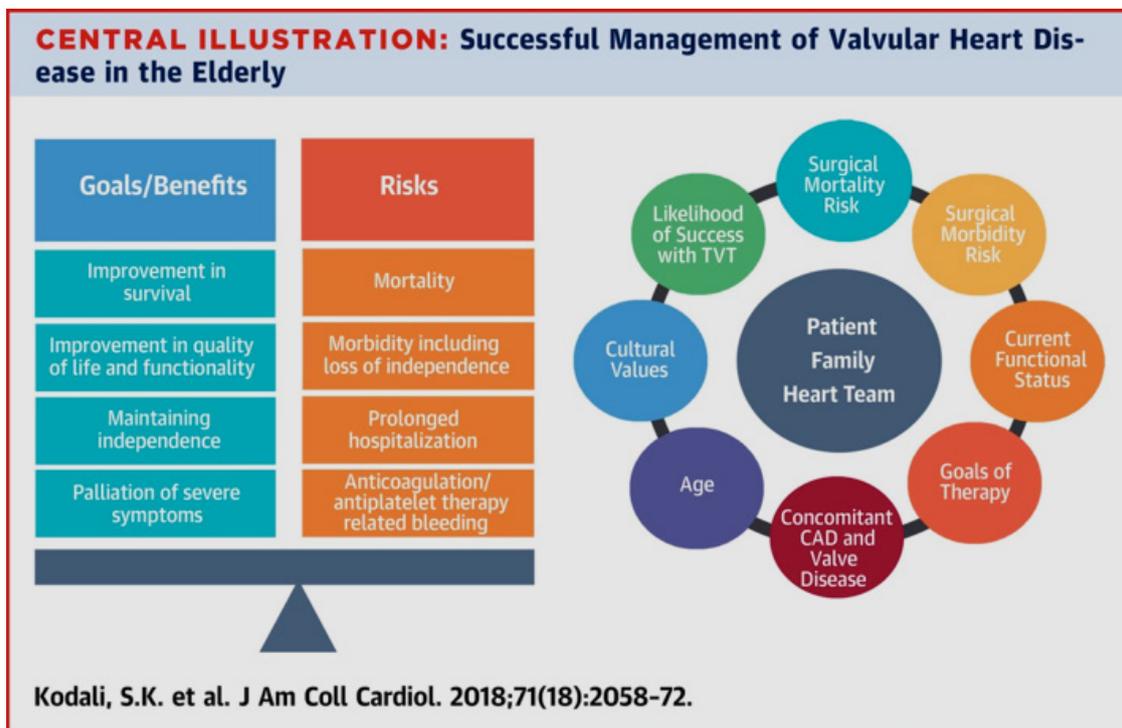
# State-of-Art Review: Aspectos Epidemiológicos, Diagnósticos e Terapêuticos da Doença Valvar após os 80 anos

## Valvular Heart Disease in Patients ≥80 Years of Age

In the United States, the octogenarian population is projected to triple by 2050. With this aging population, the prevalence of valvular heart disease (VHD) is on the rise. The etiology, approach to treatment, and expected outcomes of VHD are different in the elderly compared with younger patients. Both stenotic and regurgitant lesions are associated with unfavorable outcomes if left untreated. Surgical mortality remains high due to multiple co-morbidities, and long-term survival benefit is dependent on many variables including valvular pathology. Quality of life is an important consideration in treatment decisions in this age group. Increasingly, octogenarian patients are receiving transcatheter therapies, with transcatheter aortic valve replacement having the greatest momentum.

Transcatheter valve technology has evolved as a suitable alternative to surgery for the treatment of VHD in elderly patients. It has demonstrated improved survival in high-risk elderly patients, despite the morbidity from an invasive procedure, with a 20% reduction in absolute mortality at 1 year compared with medical therapy. As there is paucity of data in this age group, decisions about treatment need to be individualized based on specific valve pathology, comorbid conditions, and patient preferences.

In this review we discuss the etiology, epidemiology, diagnosis, and management of common valvular pathologies encountered in the octogenarian population, with a focus on transcatheter technologies.



## ***Revascularização Miocárdica do Paciente Diabético Multiarterial: Cirurgia Permanece o Melhor***

# **Diabetes and Multivessel Disease: Coronary Artery Bypass Grafting Remains King**

### **PURPOSE OF REVIEW**

Review the recently published scientific evidence to support the decision-making process of revascularization strategy in patients with diabetes mellitus (DM) and multivessel coronary artery disease (MVD).

### **RECENT FINDINGS**

Recently published observational analyses have proven the superiority of coronary artery bypass grafting (CABG) in patients presenting with other comorbidities together with DM, such as renal disease or heart failure.

### **SUMMARY**

Significant challenges and controversies surrounded the choice of the appropriate revascularization method in patients with DM and MVD over the last decades. FREEDOM trial was the first adequately powered randomized study to directly compare percutaneous coronary intervention (PCI) versus CABG in the DM population, showing the superiority of CABG in the long-term follow-up. Subsequently, other studies confirmed that CABG is also preferable over PCI in diabetic patients with particular comorbidities, such as renal failure and left ventricular dysfunction, and also in patients with type 1 DM and in the setting of an early acute coronary syndrome. Finally, in 2018, an individual level data meta-analysis reported an expressive reduction in all-cause mortality when comparing CABG versus PCI in patients with DM and MVD enrolled in the most recent clinical trials (hazard ratio 1.44, 95% confidence interval 1.20-1.74, P=0.0001).

# Revascularização com Enxertos Multiarteriais em Pacientes Diabéticos Vale a Pena? Resultados de Estudo Multicêntrico

## Incremental Value of Increasing Number of Arterial Grafts: The Effect of Diabetes Mellitus

### BACKGROUND

Multiarterial coronary grafting with two arterial grafts leads to improved survival compared with conventional single artery based on left internal thoracic artery to left anterior descending artery and saphenous vein grafts. We investigated whether extending arterialgrafting to three or more arterial grafts further improves survival, and whether such a benefit is modified by diabetes mellitus.

### METHODS

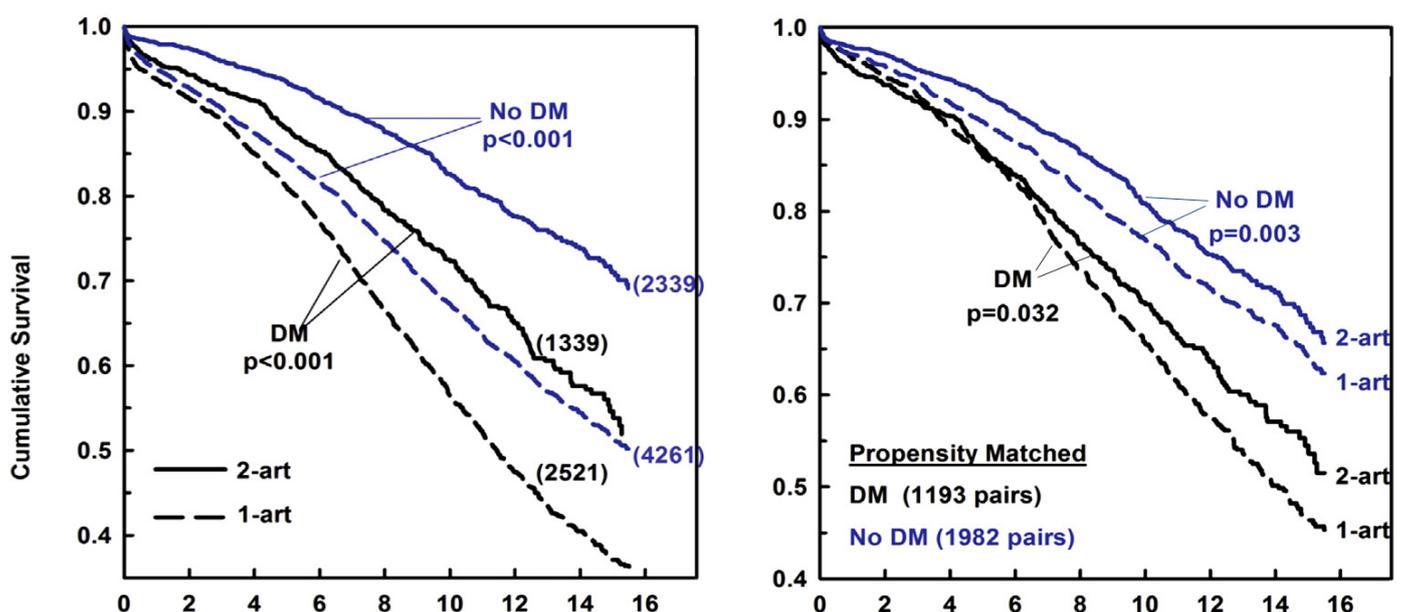
We analyzed 15-year coronary artery bypass graft surgery mortality data in 11,931 patients (age  $64.3 \pm 10.5$  years; 3,484 women [29.2%]; 4,377 [36.7%] with diabetes mellitus) derived from three US institutions (1994 to 2011). All underwent primary isolated left internal thoracic artery to left anterior descending artery grafting with at least two grafts: one artery ( $n=6,782$ ; 56.9%); two arteries ( $n=3,678$ ; 30.8%); or three or more arteries ( $n=1,471$ ; 12.3%). Long-term survival was estimated by Kaplan-Meier methods. Propensity score matching and comprehensive covariate adjustment (Cox regression) were used to derive long-term risk-adjusted hazard ratio (HR) with 95% confidence interval (CI) for increasing number of arterial grafts in the overall cohort and for diabetes and no-diabetes cohorts.

### RESULTS

Radial artery (94%) and right internal thoracic artery (6%) were used as additional arterial grafts. Multivariate analysis in all patients showed that diabetes was associated with decreased survival (HR 1.43, 95% CI: 1.34 to 1.53), whereas increasing number of arterial grafts was associated with decreased mortality (one artery HR 1.0 [reference]; two arteries HR 0.87, 95% CI: 0.80 to 0.95; and three arteries HR 0.83, 95% CI: 0.72 to 0.95). Pair wise comparisons also showed an incremental benefit of additional arterial grafts: two arteries versus one artery, HR 0.89 (95% CI: 0.80 to 0.98); and three arteries versus one artery, HR 0.80 (95% CI: 0.68 to 0.94). A three-artery versus two-artery survival advantage trend was also noted, but was not significant in either the overall study cohort (HR 0.90, 95% CI: 0.75 to 1.07), the diabetes cohort (HR 0.79, 95% CI: 0.60 to 1.03), or the no-diabetes cohort (HR 0.90, 95% CI: 0.79 to 1.26). Among diabetes patients, the survival advantage of two arteries versus one artery was modest (HR 0.96, 95% CI: 0.72 to 1.11), whereas it was significant for three arteries versus one artery (HR 0.74, 95% CI: 0.58 to 0.96). Analyses of propensity matched subcohorts were also consistent.

### CONCLUSIONS

Increasing number of arterial grafts improves long-term survival and supports extended use of arterial grafts in coronary artery bypass graft surgery, irrespective of diabetes status.



# ***Registro E-CABG Alerta para o Risco do uso de Duas Artérias Mamárias em Pacientes Idosos, Submetidos a Revascularização Miocárdica***

## **Early Outcome of Bilateral *versus* Single Internal Mammary Artery Grafting in the Elderly**

### **BACKGROUND**

Bilateral internal mammary artery (BIMA) grafting is increasingly used in elderly patients without evidence of its risks or benefits compared with single internal mammary artery (SIMA) grafting.

### **METHODS**

In all, 2,899 patients aged 70 years or older (855 [29.5%] underwent BIMA grafting) operated on from January 2015 to December 2016 and included in the prospective multicenter Outcome After Coronary Artery Bypass Grafting (E-CABG) study were considered in this analysis.

### **RESULTS**

One-to-one propensity matching resulted in 804 pairs with similar preoperative risk profile. Propensity score matched analysis showed that BIMA grafting was associated with a nonstatistically significant increased risk of in-hospital death (2.7% versus 1.6%,  $P=0.117$ ). The BIMA grafting cohort had a significantly increased risk of any sternal wound infection (7.7% versus 5.1%,  $P=0.031$ ) as well as higher risk of deep sternal wound infection/mediastinitis (4.0% versus 2.2%,  $P=0.048$ ). The BIMA grafting cohort required more frequently extracorporeal membrane oxygenation (1.0% versus 0.1%,  $P=0.02$ ), and the intensive care unit stay (mean 3.6 versus 2.6 days,  $P<0.001$ ) and in-hospital stay (mean 11.3 versus 10.0 days,  $P<0.001$ ) were significantly longer compared with the SIMA grafting cohort. Test for interaction showed that urgent operation in patients undergoing BIMA grafting was associated with higher risk of in-hospital death (5.6% versus 1.3%,  $P=0.009$ ).

### **CONCLUSIONS**

Bilateral internal mammary artery grafting in elderly patients seems to be associated with a worse early outcome compared with SIMA grafting, particularly in patients undergoing urgent operation. Until more conclusive results are gathered, BIMA grafting should be reserved only for elderly patients with stable coronary artery disease, without significant baseline comorbidities and with long life expectancy.

## Uso da Fração do Fluxo de Reserva (FFR) na Cirurgia de Revascularização Miocárdica: O que dizem as Evidências?

### Role of Invasive Functional Assessment in Surgical Revascularization of Coronary Artery Disease

Coronary artery bypass grafting (CABG) is a class I indication for revascularization of patients with multivessel or left main coronary artery disease (CAD). The decision to perform CABG is usually based on the anatomic assessment of CAD severity by coronary angiography. Although coronary angiography has good spatial and temporal resolution, it does not provide information about the functional significance of CAD.

Studies using fractional flow reserve (FFR) in patients with stable CAD with an intermediate degree of stenosis have shown that the benefit of percutaneous coronary intervention (PCI) applies only to those patients with significant ischemia on invasive functional evaluation by FFR. These studies have underlined the importance of an integrated invasive anatomic and functional evaluation of intermediate-grade lesions in patients undergoing PCI to achieve better outcomes. The instantaneous wave-free ratio (iFR) is another physiological technique for the invasive functional assessment of CAD that has shown good reproducibility and agreement with FFR.<sup>5</sup>

The role of invasive functional assessment in patients referred for CABG has not been well elucidated. Some of the lesions that are deemed significant based on anatomic assessment by angiography may not be functionally significant on invasive assessment, and this might have important clinical implications on the number and type of grafts, procedure time, graft patency rates, and, ultimately, clinical outcomes.

Integration of functional evaluation could also change the revascularization strategy (ie, PCI versus CABG) by reclassifying disease severity. In this review, we discuss the role of the physiological assessment of coronary artery lesions with invasive functional modalities in patients referred for CABG and the important implications it may have on patient selection and surgical strategy.

**Table 2. Ongoing Clinical Studies on Invasive Functional Assessment Using FFR in Patients Referred for CABG**

Clinical Trial	ClinicalTrials.gov Identifier	Study Design	No. of Patients	Primary Outcome	Follow-up	Study Limitations
FAME 3 (A Comparison of Fractional Flow Reserve-Guided Percutaneous Coronary Intervention and Coronary Artery Bypass Graft Surgery in Patients with Multivessel Coronary Artery Disease)	NCT02100722	Randomized, open label	1500	Death, MI, stroke, and any repeat revascularization	1 y	No direct assessment of role of FFR in CABG
GRAFFITI (Graft Patency After FFR-guided Versus Angio-guided CABG Trial)	NCT01810224	Prospective, randomized (1:1), multicenter, international study	206	Graft patency	1 y	No clinical outcomes Short follow-up
FARGO (Fractional Flow Reserve Versus Angiography Randomization for Graft Optimization Trial)	NCT02477371	Prospective, randomized (1:1), multicenter study	168	Graft patency	6 mo	No clinical outcomes
Impact of Preoperative FFR on Arterial Bypass Graft Functionality: Toward a New CABG Paradigm	NCT02527044	Efficacy study, open label	120	FFR	16 mo	Absence of comparator arm Short follow-up (6 mo) for graft patency Only qualitative of clinical outcome

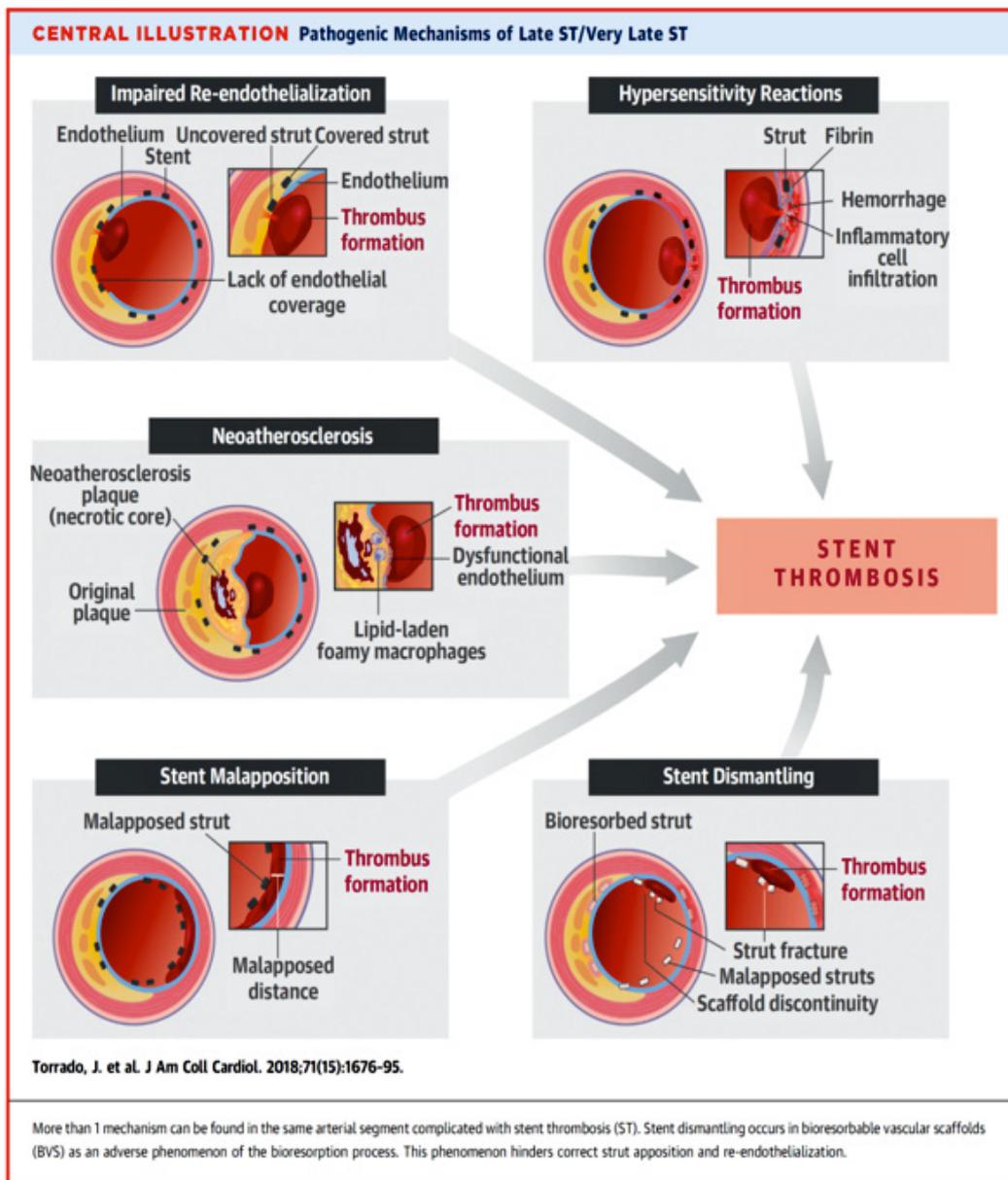
# Revisão Aborda Reestenose, Trombose e Complicações Hemorrágicas Relativas aos Stents Farmacológicos

## Restenosis, Stent Thrombosis, and Bleeding Complications

The field of interventional cardiology has significantly evolved over 40 years by overcoming several challenges. The introduction of first-generation drug-eluting stents significantly reduced the rates of restenosis, but at the expense of an increase of late stent thrombosis. Prolonged antithrombotic therapy reduced rates of stent thrombosis, but at the cost of increased bleeding. Although the advent of second-generation drug-eluting stents subsequently reduced the incidence of late stent thrombosis, its permanent nature prevents full recovery of vascular structure and function with attendant risk of very late stent failure.

In the present era of interventional cardiology, the tradeoff between stent thrombosis, restenosis, and bleeding presents as a particularly complex challenge.

In this review, the authors highlight major contributors of late/very late stent thrombosis while targeting stent restenosis, and they discuss evolutionary advances in stent technology and antiplatelet therapy, to further improve upon the care of patients with coronary artery disease.



# Estudo Americano Demonstra Redução da Taxa de Mortalidade do Infarto do Miocárdio, Durante a Época dos Congressos de Cardiologia

## Acute Myocardial Infarction Mortality During Dates of National Interventional Cardiology Meetings

### BACKGROUND

Previous research has found that patients with acute cardiovascular conditions treated in teaching hospitals have lower 30-day mortality during dates of national cardiology meetings.

### METHODS AND RESULTS

We analyzed 30-day mortality among Medicare beneficiaries hospitalized with acute myocardial infarction (overall, ST-segment-elevation myocardial infarction, and non-ST-segment-elevation myocardial infarction) from January 1, 2007, to November 31, 2012, in major teaching hospitals during dates of a major annual interventional cardiology meeting (Transcatheter Cardiovascular Therapeutics) compared with identical nonmeeting days in the ±5 weeks. Treatment differences were assessed. We used a database of US physicians to compare interventional cardiologists who practiced and did not practice during meeting dates (“stayers” and “attendees,” respectively) in terms of demographic characteristics and clinical and research productivity. Unadjusted and adjusted 30-day mortality rates were lower among patients admitted during meeting versus nonmeeting dates (unadjusted, 15.3% [482/3153] versus 16.7% [5208/31 556] [P=0.04]; adjusted, 15.4% versus 16.7%; difference -1.3% [95% confidence interval, -2.7% to -0.1%] [P=0.05]). Rates of interventional cardiologist involvement were similar between dates (59.5% versus 59.8% of hospitalizations; P=0.88), as were percutaneous coronary intervention rates (30.2% versus 29.1%; P=0.20). Mortality reductions were largest among patients with non-ST-segment-elevation myocardial infarction not receiving percutaneous coronary intervention (16.9% versus 19.5% adjusted 30-day mortality; P=0.008). Compared with stayers, attendees were of similar age and sex, but had greater publications (18.9 versus 6.3; P<0.001), probability of National Institutes of Health funding (5.3% versus 0.4%; P<0.001), and clinical trial leadership (10.3% versus 3.9%; P<0.001), and they performed more percutaneous coronary interventions annually (85.6 versus 63.3; P<0.001).

### CONCLUSIONS

Hospitalization with acute myocardial infarction during Transcatheter Cardiovascular Therapeutics meeting dates was associated with lower 30-day mortality, predominantly among patients with non-ST-segment-elevation myocardial infarction who were medically managed.

### Clinical Perspective

#### What Is New?

- Patients hospitalized with acute myocardial infarction during dates of Transcatheter Cardiovascular Therapeutics annual meetings had lower 30-day mortality compared with patients hospitalized with acute myocardial infarction during identical nonmeeting days in the ±5 weeks.
- Rates of interventional cardiologist involvement were similar between meeting and nonmeeting dates, as were percutaneous coronary intervention rates.
- Mortality reductions were largest among patients hospitalized with non-ST-segment-elevation myocardial infarction who did not receive percutaneous coronary intervention.

**Table 2.** Unadjusted 30-Day Mortality Among Patients Admitted for AMI During Dates of National Interventional Cardiology Meetings

Population	30-d Mortality, % (No. of Events/No. at Risk)		P Value
	Cardiology Meeting Dates	Nonmeeting Dates	
All patients	15.3 (482/3153)	16.7 (5208/31 156)	0.04
Patients with STEMI, overall	22.6 (116/514)	20.9 (1052/5026)	0.39
Received PCI during hospitalization	8.4 (23/273)	9.3 (241/2588)	0.63
Did not receive PCI during hospitalization	38.6 (93/241)	33.3 (811/2438)	0.10
Patients with NSTEMI, overall	13.9 (366/2639)	15.9 (4156/26 130)	0.006
Received PCI during hospitalization	5.0 (34/680)	5.0 (322/6487)	0.97
Did not receive PCI during hospitalization	16.9 (332/1959)	19.5 (3834/19 643)	0.006

## Comparação da Resposta Microcirculatória à Circulação Extracorpórea com Fluxos Pulsado ou Contínuo

# Microvascular Responsiveness to Pulsatile and Nonpulsatile Flow During Cardiopulmonary Bypass

### BACKGROUND

Pulsatile perfusion may offer microcirculatory advantages over conventional nonpulsatile perfusion during cardiopulmonarybypass (CPB). Here, we present direct visual evidence of microvascular perfusion and vasoreactivity between perfusion modalities.

### METHODS

A prospective, randomized cohort study of 20 high-risk cardiac surgical patients undergoing pulsatile (n=10) or nonpulsatile (n=10) flow during CPB was conducted. Changes in sublingual mucosal microcirculation were assessed with orthogonal polarization spectral imaging along with near-infrared spectroscopic indices of thenar muscle tissue oxygen saturation (StO<sub>2</sub>) and its recovery during a vascular occlusion test at the following time points: baseline (T<sub>0</sub>), 30 minutes on CPB (T<sub>1</sub>), 90 minutes on CPB (T<sub>2</sub>), 1 hour after CPB (T<sub>3</sub>), and 24 hours after CPB (T<sub>4</sub>).

### RESULTS

On the basis of our scoring scale, a shift in microcirculatory blood flow occurred over time. The pulsatile group maintained normal perfusion characteristics, whereas the nonpulsatile group exhibited deterioration in perfusion during CPB (T<sub>2</sub>: 74.0% ± 5.6% versus 57.6% ± 5.0%) and after CPB (T<sub>3</sub>: 76.2% ± 2.7% versus 58.9% ± 5.2%, T<sub>4</sub>: 85.7% ± 2.6% versus 69.8% ± 5.9%). Concurrently, no important differences were found between groups in baseline StO<sub>2</sub> and consumption slope at all time points. Reperfusion slope was substantially different between groups 24 hours after CPB (T<sub>4</sub>: 6.1% ± 0.6% versus 3.7%±0.5%), indicating improved microvascular responsiveness in the pulsatile group versus the nonpulsatile group.

### CONCLUSIONS

Pulsatility generated by the roller pump during CPB improves microcirculatory blood flow and tissue oxygen saturation compared with nonpulsatile flow in high-risk cardiac surgical patients, which may reflect attenuation of the systemic inflammatory response and ischemia-reperfusion injury.

Table 6. Lactate and Creatinine Levels

Variable	T <sub>0</sub>	T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub>	T <sub>4</sub>
Lactate, mEq/L					
Pulsatile group	1.4 (0.8–1.9)	1.6 (1.2–2.4)	1.8 (1.6–2.4) <sup>b</sup>	2.4 (1.7–3.5) <sup>b</sup>	1.2 (1.1–1.3)
Nonpulsatile group	1.0 (0.9–1.1)	1.3 (1.1–2.1) <sup>b</sup>	1.4 (1.2–2.1) <sup>b</sup>	2.6 (2.0–4.4) <sup>b</sup>	1.9 (1.3–2.5) <sup>b</sup>
Creatinine, μmol/L					
Pulsatile group	80 (61–96)	NA	NA	76 (62–104)	76 (58–110)
Nonpulsatile group	89 (78–119)	NA	NA	92 (78–121)	117 (90–182) <sup>a</sup>

<sup>a</sup>  $p < 0.05$  versus pulsatile group. <sup>b</sup>  $p < 0.05$  versus T<sub>0</sub>, by post hoc comparisons.