



CONTROVERSES ET ACTUALITES EN CHIRURGIE VASCULAIRE

CONTROVERSIES & UPDATES IN VASCULAR SURGERY

**JANUARY 23-25 2020**



MARRIOTT RIVE GAUCHE & CONFERENCE CENTER | PARIS | FRANCE

Paclitaxel crisis-where are we?



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## Disclosure

Speaker name: Scott Trerotola

.....

I have the following potential conflicts of interest to report:

Consulting: BD Bard, B Braun, Cook, Teleflex, Adrenas,  
WL Gore, MedComp

Royalty, Cook and Teleflex



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- Paclitaxel “crisis”? What crisis?
- PAD concerns-yes
- Dialysis access use-no
- Guilt by association-maybe
- Effect on industry-yes
- Effect on research-yes



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## Risk of Death Following Application of Paclitaxel-Coated Balloons and Stents in the Femoropopliteal Artery of the Leg: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Konstantinos Katsanos, MD, PhD, MSc, EBIR; Stavros Spiliopoulos, MD, PhD; Panagiotis Kitrou, MD, PhD; Miltiadis Krokidis, MD, PhD; Dimitrios Karnabatidis, MD, PhD

Treatment of **Peripheral Arterial Disease** with Paclitaxel-Coated Balloons and Paclitaxel-Eluting Stents Potentially Associated with Increased Mortality - Letter to Health Care Providers

UPDATE: Treatment of **Peripheral Arterial Disease** with Paclitaxel-Coated Balloons and Paclitaxel-Eluting Stents Potentially Associated with Increased Mortality - Letter to Health Care Providers

UPDATE: Treatment of **Peripheral Arterial Disease** with Paclitaxel-Coated Balloons and Paclitaxel-Eluting Stents Potentially Associated with Increased Mortality

November 2018

US FDA January 2019

US FDA March 2019

US FDA August 2019



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Editorial

## Use of Paclitaxel-Eluting Technologies in the Femoropopliteal Segment Under Scrutiny Over Possible Link to Late All-Cause Mortality: Time to Panic or an Opportunity to Resurge?

JOURNAL OF  
**ENDOVASCULAR**  
THERAPY  
A SAGE Publication

Journal of Endovascular Therapy  
2019, Vol. 26(1) 41–43  
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DOI: 10.1177/1526602818824682  
www.jevt.org  
SAGE

Cardiovasc Intervent Radiol (2019) 42:1050–1052  
<https://doi.org/10.1007/s00270-019-02225-6>



COMMENTARY

## The Truth on Paclitaxel and the Mysterious Ways of Data Interpretation?

Jos C. van den Berg<sup>1,2</sup>

Cardiovasc Intervent Radiol (2019) 42:1508–1509  
<https://doi.org/10.1007/s00270-019-02297-4>



COMMENTARY

## Commentary on Drug-Eluting Technologies

Trevor Cleveland<sup>1</sup> · Lars Lonn<sup>2</sup> · Dierk Vorwerk<sup>3</sup>



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- Debate rages on in PAD community
  - Difficult to imagine that a single dose of drug could affect mortality
- What about hemodialysis population?
  - High mortality at baseline
  - Lower dose of drug (much shorter balloons)
  - However, might be applied multiple times
  - Much more limited dataset with only 2 year FU



## Original Clinical Studies

Mortality After Paclitaxel-Coated Device  
Use in Dialysis Access: A Systematic  
Review and Meta-Analysis

Krystal Dinh, BMed, MTrauma<sup>1</sup>, Alexandra M. Limmer, MBBS, MS<sup>2</sup>,  
Sharath C. V. Paravastu, MBBS, PGDip, MD, FRCS<sup>3</sup>,  
Shannon D. Thomas, BSc Med Hons, MBBS, FRACS<sup>4,5,6</sup>,  
Michael H. Bennett, MBBS, FANZCA, MD<sup>5,7</sup>,  
Andrew Holden, MBChB, FRANZCR, EBIR<sup>8</sup>,  
and Ramon L. Varcoe, MBBS, MS, FRACS, PhD<sup>4,5,6</sup>

“The analysis found no difference in short- to midterm mortality among patients treated with a drug-coated balloon compared with PTA. With proven benefit and no evidence of harm, the authors recommend ongoing use of PCB for the failing dialysis access.”

JOURNAL OF  
ENDOVASCULAR  
THERAPY

Journal of Endovascular Therapy  
1-13

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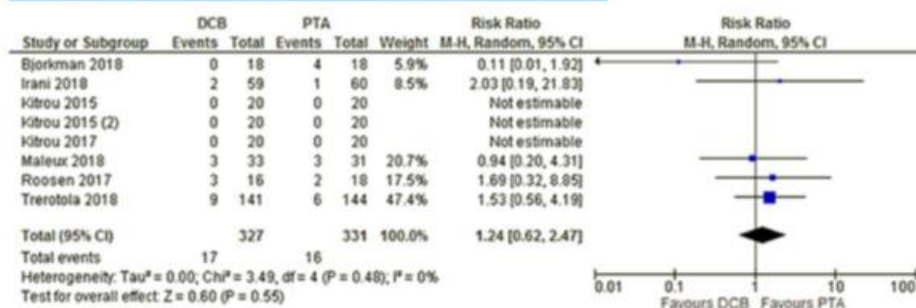
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DOI: 10.1177/1526602819872154

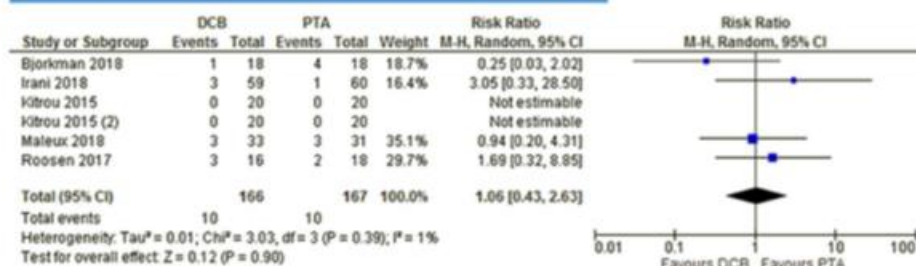
www.jevt.org



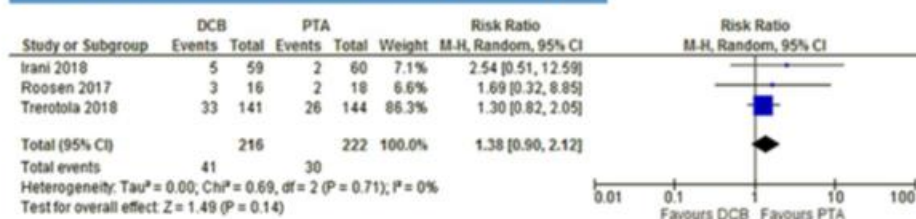
## A. 6-Month All Cause Mortality



## B. 12-Month All Cause Mortality



## C. 24-Month All Cause Mortality





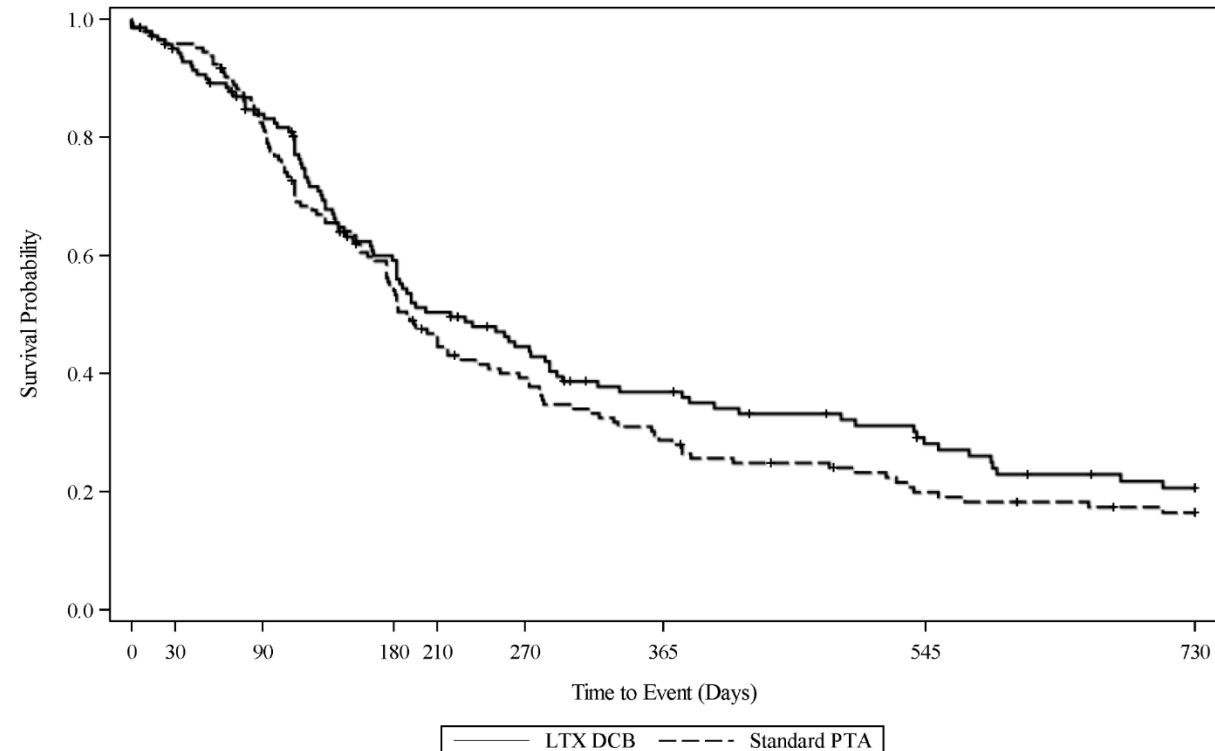


## Lutonix **AV** Clinical Trial-24 Month Safety

RCT, n=285

PTA vs DCB after successful vessel prep

All AVF







Description	Lutonix (n=141)	Control (n=144)	P value
Number of deaths at 24 months	33 (23.4%)	26 (18.1%)	<b>P=0.265</b>

N= 4 voluntarily withdrew from dialysis- Lutonix

N=1 voluntarily withdrew from dialysis- control

Expected 2 year mortality on hemodialysis  
(US) 33.2%<sup>1</sup>

<sup>1</sup>USRDS Table 5.3 Adjusted survival percentage v2 Mortality 18, 66.8% survival at 24 months

	Lutonix (n=141)	Control (n=144)
ESRD (inc hyperkalemia)	5	5
Cardiovascular	14	13
Respiratory failure/pneumonia	2	1
Sepsis	2	0
Unknown/natural causes	2	1
Neurological event	2	1
Hospice		1
Postoperative PEA arrest	1	
Ischemic colitis	1	
Voluntary withdrawal from dialysis	3	1
Malignancy	1	2
Complications of diabetes		1
Total	33	26



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University of Pennsylvania Health System Department of  
Radiology  
Division of Interventional Radiology

Consent for Dialysis Fistulogram and Possible Angioplasty, Stent or Stent-graft Placement or Thrombolytic  
Therapy (*Bare balloon/stent only*)

University of Pennsylvania Health System Department of  
Radiology  
Division of Interventional Radiology

Consent for Dialysis Fistulogram and Possible Angioplasty, Stent or Stent-graft Placement or Thrombolytic  
Therapy



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”Some studies have suggested that there is an increased risk of death in patients who undergo treatment for peripheral arterial disease in the femoropopliteal artery with paclitaxel-coated stents and balloons compared to patients treated with uncoated devices. The FDA has advised that the relationship, if any, between the use paclitaxel-coated stents and balloons and patient deaths requires further study.”

Local impact? Nearly all patients sign this consent (PAD and HD), very few opt out.





- Society Recommendations

- SCAI “It is important to note that SCAI believes the associations are hypothesis-generating and require further investigation with patient-level data”
- CIRSE “In the majority... alternatives to drug-eluting devices should be used...For some ...high risk for restenosis...benefits of using a paclitaxel-coated device may outweigh the risks...full informed consent process...patients who have already received paclitaxel-eluting devices should be followed (for) mortality”



- Global Impact (hemodialysis access)?
  - Some clinical trials folded/went on hiatus
  - Others enrolling much more slowly (Lutonix AV enrolled in 9 months)
  - Overall markedly decreased use (? 50%) in spite of lack of evidence

ClinicalTrials.gov Identifier: NCT03189667

Recruitment Status ☐ : Terminated (slow recruitment and recent concerns of safety of Paclitaxel coated balloons and associated increased risk death)

First Posted ☐ : June 16, 2017

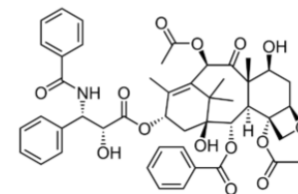
Last Update Posted ☐ : May 1, 2019

NEWS • INTERVENTIONAL

## Two Trials Halted in Wake of Study Linking Paclitaxel-Coated Devices to Deaths in PAD

[Reaction to the Katsanos et al meta-analysis](#)

6th December 2019 ☐ 1019



Paclitaxel

[SWEDEPAD 1 and SWEDEPAD 2 trials halt inclusion after Katsanos et al's meta-analysis on paclitaxel-coated devices and interim safety analysis](#)

11th December 2018 ☐ 1530

*Interventional News* has learned that inclusion into the [SWEDEPAD](#) studies, that are examining benefits of drug-eluting technology for peripheral arterial disease patients, has been halted.

(Restarted after own analysis)

FDA's advisory panel meeting in June, convened to address a safety signal in paclitaxel-coated balloons and stents in peripheral interventions, has stalled the market. BD in May [cut its earnings guidance](#) in anticipation of a 50% drop in sales of its drug-coated balloons.



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## EVIDENCE-BASED REVIEW

Hot off the presses: January 14, 2020 JVIR on-line

### **Risk of Death and Amputation with Use of Paclitaxel-Coated Balloons in the Infrapopliteal Arteries for Treatment of Critical Limb Ischemia: A Systematic Review and Meta-Analysis of Randomized Controlled Trials**

Konstantinos Katsanos, MD, MSc, PhD, Stavros Spiliopoulos, MD, PhD,  
Panagiotis Kitrou, MD, PhD, Miltiadis Krokidis, MD, PhD,  
Ioannis Paraskevopoulos, MD, PhD, and Dimitrios Karnabatidis, MD, PhD

Amputation-free survival worse with paclitaxel (13.7% crude risk of death or limb loss compared to 9.4% in case of uncoated balloon angioplasty; hazard ratio 1.52; 95% confidence interval: 1.12–2.07,  $p=0.008$ )

TLR reduced with paclitaxel (11.8% crude risk of TLR versus 25.6% in control; risk ratio 0.53; 95% confidence interval: 0.35–0.81,  $p=0.004$ ).

Harm signal evident with high-dose (3.0-3.5  $\mu\text{g}/\text{mm}^2$ ) devices, below significance in case of a low-dose (2.0  $\mu\text{g}/\text{mm}^2$ ) device





- Where are we (hemodialysis)?
  - Exciting new efficacy data (in.Pact)
  - No mortality signal
  - Competing devices (stent grafts-Avenew)
  - Getting back to normal or “new normal”
  - More (long term) data coming