

## Cardiac Update 2016-2017

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*I have no financial disclosures or affiliations*

### Learning Objectives

- Pharmacology for cardiac procedures
- TAVR: What's the latest?
- New procedures you may be doing
- Atrial Fibrillation- Is it rate or rhythm?
- Blood transfusion- What's the limit? What can we add?
- Grab Bag of info

### Pharmacology

- Cardiac Anesthesia
  - Definition of polypharmacy
  - Neurocognitive outcomes
  - Aging population
  - Fast track patients
- Do we make a difference?
  - CPB times
  - Embolic CVA
  - Transfusions

### Dexmedetomidine Use

- Several prior studies showing improved outcomes in cardiac surgery
  - Mortality: In house, 30d, 1 yr
  - Neurologic : Delirium
  - Renal outcomes
- Recent publications in non-cardiac surgery
  - Reduced delirium post op in elderly patients
  - Safety in sedation of elderly with cognitive impairments

#### **Dexmedetomidine versus Propofol Sedation Reduces Delirium after Cardiac Surgery**

*A Randomized Controlled Trial*

George Djilani, M.D., F.R.C.A., F.R.C.P.C., Natalie Silverton, M.D.,  
Ludwik Fedorko, M.D., Ph.D., F.R.C.P.C., Jo Carroll, B.H.A., Rima Styra, M.D., F.R.C.P.C.,  
Vivek Rao, M.D., Ph.D., F.R.C.P.C., Rita Katznelson, M.D.

**ANESTHESIOLOGY 2016; 124:362-8**

- Prospective, randomized, controlled trial of Dex vs Propofol
- Addressed heterogeneity of data on delirium
  - Delirium as primary outcome
- 185 patients randomized

## Study Methods

- Patients > 60 yo with elective complex surgery
- Patients >70 yo with CABG or single valve surgery
- Standardized anesthetic
  - Midazolam limited to 0.05 mg/kg max
- Sedation initiated on ICU arrival
  - Dex bolus + infusion – not DC'ed on extubation
- Ventilation > 24 hrs: Dex converted to propofol
- Multimodal analgesia

## Results

Table 2. Onset and Duration of Delirium and the Length of Stay in Patients with Delirium

	Dexmedetomidine Group (n = 16)	Propofol Group (n = 29)	P Value
Onset of delirium, d, median (range)	2 (1–4)	1 (1–4)	0.027
Duration of delirium, d, median (range)	2 (1–4)	3 (1–5)	0.04
Extubation time, h, median (range)	5.5 (3.5–14.3)	7.8 (3.8–202.2)	0.0007
Intensive care unit length of stay, h, median (range)	67.8 (20–214)	76.5 (17.8–956.5)	0.38
Hospital length of stay, d, median (range)	7.5 (5–32)	10 (6–74)	0.054

Table 4. Delirium, Sedation, and Pain Scores and Requirements for Analgesia and Antipsychotics in Dexmedetomidine and Propofol Groups

	Dexmedetomidine Group (n = 91)	Propofol Group (n = 92)	P Value
Delirium frequency, n (%)	16 (17.5)	29 (31.5)	0.028
Haloperidol, n (%)	12 (13)	24 (26)	0.04
Quetiapine, n (%)	3 (3.3)	5 (5.4)	0.72
Sedation Agitation Scale scores, 24 h	4 (1–7)	4 (1–7)	0.13

## Summary

- Post Op Delirium (POD)
  - Dex 17.5% vs Prop 31.5%
- Duration of delirium (median days)
  - Dex 2d vs Prop 3d
- Hospital LOS (median days)
  - Dex 7.5 vs Prop 10
- Delirium related hours
  - 450 vs 1200 (ICU) and 532 vs 888 (floor) for Dex vs Prop

## The Effect of Dexmedetomidine on Outcomes of Cardiac Surgery in Elderly Patients



Hao Cheng, MD,<sup>1\*</sup> Zhongmin Li, PhD,<sup>2</sup> Nilas Young, MD,<sup>3</sup> Douglas Boyd, MD,<sup>3</sup> Zane Atkins, MD,<sup>3</sup> Fuhai Ji, MD,<sup>4</sup> and Hong Liu, MD<sup>1</sup>

*Journal of Cardiothoracic and Vascular Anesthesia*, Vol 30, No 6 (December), 2016; pp 1502–1508

- Retrospective, single center
- 505 patients
- Authors reviewed 5 years of data for elderly patients
- CABG or Valve/CABG > 65 years old
- Dexmedetomidine vs Non-Dex groups

## Methodology

- Univariate and multivariate regression analysis
  - Demographic, therapeutic, and clinical outcome variables
- Propensity score
  - Likelihood of a patient receiving Dex
- Dex group : More CRF, CHF, lipid lowering agents
  - Less urgent surgery, CVD and lower BMI
  - Shorter CPB, X-clamp times, less IABP use

## Take Away Message

- Data consistent with prior studies
  - Same dataset as previously published work
- Improved in hospital and 30d mortality benefit
  - 1 year mortality benefit did not persist in elderly
- Decreased stroke risk
- Decreased delirium
  - Very low rates of delirium reported in this study

**Sevoflurane Versus Total Intravenous Anesthesia for Isolated Coronary Artery Bypass Surgery With Cardiopulmonary Bypass: A Randomized Trial**



Valery V. Likhvantsev, MD,\* Giovanni Landoni, MD,† Dmitry I. Levikov, PhD,‡ Oleg A. Grebenchikov, PhD,\* Yuri V. Skripkin, MD,\* and Rostislav A. Cherpakov, MD†

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- Randomized controlled trial, 2 hospitals
- Isolated CABG in native chest
- TIVA vs volatile anesthetic maintenance
- 900 patients randomized 2012-2014

## Details

- Volatile group
  - Allowed for propofol during induction (38% without propofol)
  - Fentanyl, sevoflurane, cisatracurium intermittent bolus
- TIVA group
  - Propofol gtt, fentanyl intermittent, and cisatracurium
- No benzodiazepines or etomidate use reported in either

**Table 2. Cardiac Biomarkers and Length of Hospital Stay in Patients Randomly Assigned to Receive Propofol-Based Total Intravenous Anesthesia or Sevoflurane**

	TIVA Group (n = 439)	Sevoflurane Group (n = 439)	P Value
Troponin T after 24 h, ng/mL	0.57 (0.12-0.91)	0.18 (0.12-0.35)	<0.001
NT-proBNP after 24 h, pg/mL	878 (561-1,825)	633 (452-1,105)	<0.001
NT-proBNP after 48 h, pg/mL	1,036 (692-2,496)	482 (240-854)	<0.001
Hospital stay, days	14 (10-16)	10 (8-11)	<0.001
Hospital stay in survivors, days	14 (11-16)	10 (8-11)	<0.001

NOTE. Data are presented as median (interquartile range).  
Abbreviations: NT-proBNP, N-terminal pro-brain natriuretic peptide; TIVA, total intravenous anesthesia.

Subgroup	7-day Mortality	1-month Mortality	1-year Mortality	Hospital Stay	Troponin T After 24 h, ng/mL	NT-proBNP After 24 h, pg/mL	NT-proBNP After 48 h, pg/mL
With propofol, n = 700	2.0%	4.7%	22.7%	11 (10-14)	0.36 (0.13-0.78)	807 (505-1,574)	711 (514-1,542)
Without propofol, n = 168	0%	2.4%	16.5%	10 (8-10)	0.18 (0.11-0.30)	547 (363-880)	432 (228-668)
p value	0.085	0.21	0.15	<0.001	<0.001	<0.001	<0.001

NOTE. Data are presented as percentages or as median (interquartile range).  
Abbreviation: NT-proBNP, N-terminal pro-brain natriuretic peptide.

## Conclusions

- Largest randomized trial of volatile vs TIV anesthetic
- Decreased post-op TroponinT
- Decreased proBNP
- Decreased hospital LOS
- Increased biomarkers and LOS if propofol was used during induction in
  - Trend towards mortality benefit at all points

Can J Anaesth Can Anesth (2016) 63:1128-1139  
DOI 10.1007/s12630-016-0796-y



**REPORTS OF ORIGINAL INVESTIGATIONS**

**Comparison of isoflurane and sevoflurane in cardiac surgery: a randomized non-inferiority comparative effectiveness trial**

Philip M. Jones, MD · Daniel Bainbridge, MD · Michael W. A. Chu, MD · Philip S. Fernandes, BA · Stephanie A. Fox, BA · Ivan Iglesias, MD · Bob Kihal, MD · Ronit Lavi, MD · John M. Murkin, MD

- Pragmatic randomized, non-inferiority study
- CABG or single valve study, 464 patients
- 2011-2014
- Single center

## Simple Answer

- There was no difference!
- Primary Outcome: Prolonged ICU stay or 30d mortality
  - Trend towards Sevo better for prolonged ICU stay
- Clinically irrelevant cTnT and Cr elevation with Sevo
- Cost Analysis:
  - Sevo: \$41 (Canadian \$)
  - Iso: \$5

## Etomidate

- The story continues....
- Known adrenocortical insufficiency with single doses
  - Clinically relevant?
- Periop concerns for hemodynamic instability and infection
- Potential modulation of inflammation
  - Increased IL-6 and without compensatory anti-inflammation
- Authors question relationship for atrial fibrillation
  - A Fib admittedly multifactorial

## Etomidate and the Risk of Complications After Cardiac Surgery: A Retrospective Cohort Analysis



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*Journal of Cardiothoracic and Vascular Anesthesia*, Vol 30, No 6 (December), 2016; pp 1516-1522

- Retrospective cohort study with propensity matching
- 8,978 patients undergoing CABG or CABG/valve
- Etomidate: Other induction agents in 2:1 matched study
- Primary outcome: Rates of A Fib, LOS
- Secondary Outcomes: Bleeding and major complications

Table 2. Results for the Primary Outcomes

Primary Outcome	Etomidate (n = 4,094)	Non-etomidate (n = 2,824)	Estimated OR (95% CI) <sup>†</sup> (ORs or IRRs)	P <sup>‡</sup>
Postoperative atrial arrhythmia, yes (%)	33.4	31.5	1.07 (0.92, 1.23) <sup>†</sup>	0.29
Length of ICU stay (hours)	28.0 [23.4, 55.1]	27.4 [23.5, 50.1]	1.00 (0.94, 1.06) <sup>†</sup>	0.98
Length of hospital stay (days)	7.3 [5.3, 11.5]	7.2 [5.3, 11.0]	1.00 (0.94, 1.06) <sup>†</sup>	0.98

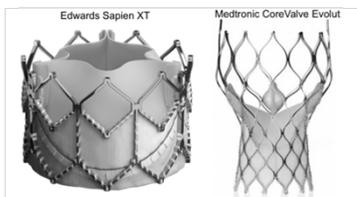
Table 3. Results for the Secondary Outcomes

Secondary Outcome (%)	Etomidate (n = 4,094)	Non-etomidate (n = 2,824)	Odds Ratio (95% CI) <sup>†</sup>	P <sup>‡</sup>
Packed red cells	20.1	16.4	1.32 (1.02, 1.70)	0.002
Fresh frozen plasma	4.2	2.9	1.44 (0.91, 2.27)	0.02
Platelets	9.8	7.6	1.29 (0.97, 1.73)	0.01
Cryoprecipitate	0.5	0.5	0.94 (0.25, 2.92)	0.97
Postoperative complications				
Cardiovascular <sup>§</sup>	2.1	2.0	0.96 (0.57, 1.61)	0.89
Reoperation	4.7	5.8	0.76 (0.55, 1.06)	0.02
Infectious	2.0	1.8	1.08 (0.63, 1.86)	0.68
Neurologic	1.5	1.4	1.06 (0.57, 1.97)	0.78
Pulmonary	10.1	9.6	0.99 (0.77, 1.29)	0.94
Renal	3.5	3.6	0.90 (0.60, 1.35)	0.45
Hematologic	0.8	0.6	1.30 (0.53, 3.21)	0.40
Gastrointestinal	2.4	1.7	1.32 (0.77, 2.25)	0.14

## Conclusions

- Atrial fibrillation rates no different
- ICU and hospital LOS also the same
- Secondary outcomes
  - Increased RBC use with etomidate
  - Trend towards increased FFP and platelets
- Limitations
  - Observational trial
  - Selection bias

## TAVR: What's the latest?



## TAVR – Long term followup

- TAVR implantation > 5 yrs ago (5-14 yrs) in 2002-2011
- 2 centers
- Cribier Edwards, Edwards SAPIEN, SAPIEN XT valves
- 704 TAVI cases, 378 with long term followup
- Degeneration
  - Mean gradient  $\geq$  20mmHg without endocarditis
  - Moderate AI

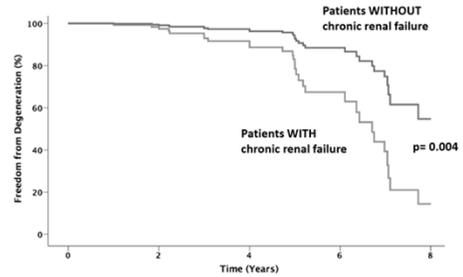
Dvir D. First look at long-term durability of transcatheter heart valves: Assessment of valve function up to 10 years after implantation. EuroPCR 2016; May 17, 2016; Paris, France



## TAVR followup

- Valve types
  - C-E: 14.3%, Edwards Sapien 49.7%, Sapien XT 36%
- Access Route
  - Transfemoral 68.5%, Transapical 28.7%
- Median Survival Time: 51 months (4 yrs, 3 mo)
- Approximately 50% degeneration at 8 years
  - CRF strongest correlation with degeneration
  - About 2/3 AI and 1/3 AS

## Long Term TAVR follow up



### Original Article Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

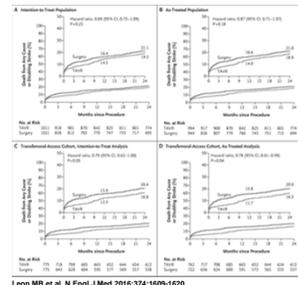
Martin B. Leon, M.D., Craig R. Smith, *et al.* for the PARTNER 2 Investigators

N Engl J Med  
Volume 374(17):1609-1620  
April 28, 2016

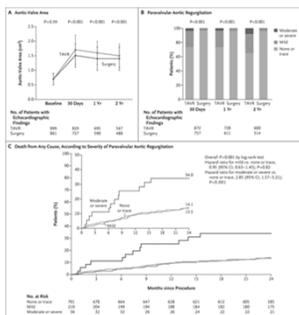
In a randomized trial involving more than 2000 patients, transcatheter aortic-valve replacement was noninferior to surgical replacement in the primary end point of death from any cause or disabling stroke at 2 years.



### Time-to-Event Curves for the Primary Composite End Point.



### Echocardiographic Findings.



Leon MB *et al.* N Engl J Med 2016;374:1609-1620



## Take Away Points

- TAVR non-inferior to surgery in intermediate risk patients
- Valve gradients were lower in TAVR than SAVR
- Paravalvular leaks greater with TAVR than SAVR
  - Moderate-Severe PVL with Hazard Ratio 2.85
- TAVR had lower bleeding risks, atrial fibrillation, AKI
- Length of Stay
  - ICU 2 vs 4 days – favoring TAVR
  - Hospital 6 vs 9 days – favoring TAVR

Have you ever seen a passive CT surgeon?  
They will not go away quietly

## Sutureless Valve Technology



Figure 1 Commercially available sutureless aortic valves. (A) F Enable (Medtronic, Minneapolis, USA); (B) Perceval S (Sorin, Sublegno, Italy); (C) Innovalve (Edward Lifesciences, Irvine, USA).

- Pericardial biologic prostheses that require less than 3 sutures
- Still requires Aortic x-clamp and CPB
- Diseased valve removed and prosthesis implants under direct vision
- CPB and X-clamp times reported are approximately half of STS averages
- Reduced PVL vs TAVR

Ann Cardiothorac Surg 2015;4(2):123-130

## SUAVR Data

- SUAVR vs Conventional AVR (C-AVR)
  - Outcomes differences yet to be reported
  - Consistently significant CPB and X-clamp times across studies
  - Shorter LOS and potential cost benefit
- 1 randomized trial of SUAVR vs C-AVR
  - Shorter x-clamp times, similar CPB
  - No differences in early outcomes
  - Improved mean gradient in SUAVR

Ann Cardiothorac Surg 2015;4(2):123-130

## TAVI vs SUAVR

Original Article

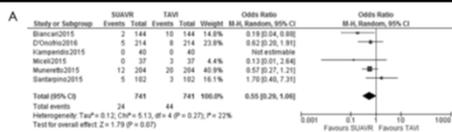
Transcatheter aortic valve implantation (TAVI) versus sutureless aortic valve replacement (SUAVR) for aortic stenosis: a systematic review and meta-analysis of matched studies

Nelson Wang<sup>1</sup>, Yi-Chin Tsai<sup>2</sup>, Natasha Nilek<sup>3</sup>, Vakhang Tchekachidishvili<sup>4</sup>, Marco Di Eusanio<sup>5</sup>, Tristan D. Yan<sup>6</sup>, Kevin Phan<sup>7</sup>

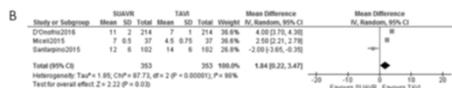
J Thorac Dis 2016;8(11):3283-3293

- Meta-analysis of TAVI vs SUAVR
- Primary outcomes paravalvular leak, short, and intermediate mortality
- 6 studies met inclusion criteria
- Compared TAVI to SUAVR via propensity score matching

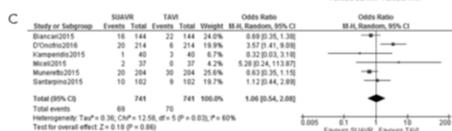
### Mortality



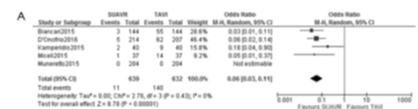
### Hospital LOS



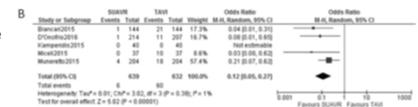
### Pacemaker



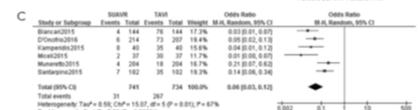
### Mild PVL



### Moderate-Severe



### Any PVL



## TAVR Anesthetic Implications and safety

- General anesthesia initially preferred choice
  - Airway management
  - Immobility during deployment
  - TEE guidance
  - Duration of initial procedures
  - Learning curve for the room
- Safety, cost containment, neurological outcomes
  - MAC as an alternative

## Outcome After General Anesthesia Versus Monitored Anesthesia Care in Transfemoral Transcatheter Aortic Valve Replacement

Paolo D'Elia, MStat,<sup>1</sup> Marco Ranucci, MD,<sup>1</sup> Remo Daniel Cavelli, MD,<sup>1</sup> Fausto Bianchi, MD, PhD,<sup>1</sup> Stefano Rosato, MStat,<sup>1</sup> Marco Barbati, MD,<sup>1</sup> Francesco Onorati, MD, PhD,<sup>1</sup> Corrado Tamburini, MD, PhD,<sup>1</sup> Gennaro Santoro, MD,<sup>1</sup> Claudio Grossi, MD,<sup>1</sup> Francesco Santini, MD,<sup>1</sup> Kalla Bontempi, MStat,<sup>1</sup> Danilo Fusco, MStat,<sup>1</sup> and Fulvia Soccaecia, MSc<sup>1</sup>, on behalf of the OBSERVANT Research Group

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- Secondary analysis from observational and prospective OBSERVANT trial
- Multicenter trial in Italy 2010-2012
- 1494 patients undergoing transfemoral TAVR
- Propensity score matching 310 pairs of MAC vs GA

## Methods

- Sapien XT (Edwards Life-Science, Irvine, CA)
- CoreValve (Medtronic, Minneapolis, MN)
- Primary Endpoint: All cause mortality
- Secondary Endpoint: Adverse events
- Propensity score matching
- MAC 1137 (76.1%) vs GA 357 (23.9%)

## Results

- No primary end point differences
- Severe paravalvular leak in 2 MAC patients, 0 in GA
- 3 year survival the same
- No methodology for MAC
- No commentary on intra-procedure adverse events

Table 3. Early Outcomes in Propensity-Score-Matched Pairs of Patients Undergoing Transcatheter Aortic Valve Replacement Under MAC Versus GA

	MAC	GA	P
	n = 1137	n = 357	Value
In-hospital mortality	12 (3.9)	15 (4.8)	0.564
30-day mortality	4 (1.3)	2 (0.7)	0.414
Stroke	5 (1.6)	6 (1.9)	0.729
Cardiogenic shock	5 (1.6)	9 (3.0)	0.285
Cardiac tamponade	12 (3.9)	7 (2.3)	0.251
Permanent pacemaker	58 (19.1)	45 (14.8)	0.168
Major vascular damage	28 (8.8)	24 (7.0)	0.758
Infection	19 (6.4)	24 (8.1)	0.411
Emergency percutaneous coronary intervention	1 (0.3)	2 (0.7)	0.564
Severe bleeding <sup>a</sup>	95 (11.8)	114 (38.1)	0.102
Paravalvular regurgitation			
Mild	121 (41.3)	134 (45.7)	0.858
Moderate	22 (7.5)	33 (11.3)	
Severe	2 (0.7)	0	
Acute kidney injury <sup>b</sup>	81 (28.2)	72 (25.2)	0.387
Acute kidney injury Network stages			
Stage 1 <sup>c</sup>	51 (17.8)	47 (16.4)	0.669
Stage 2 <sup>c</sup>	12 (4.2)	7 (2.4)	
Stage 3 <sup>c</sup>	18 (6.3)	18 (6.3)	
De novo dialysis <sup>d</sup>	13 (4.4)	16 (5.4)	0.576
Mean transvalvular gradient (mmHg)	8.7 ± 5.6	8.7 ± 4.2	0.965
Peak transvalvular gradient (mmHg)	18.3 ± 10.1	18.5 ± 8.0	0.635
Intensive care unit stay (days)	2.9 ± 4.7	3.5 ± 4.5	0.086

## Comparison of sedation and general anaesthesia for transcatheter aortic valve implantation on cerebral oxygen saturation and neurocognitive outcome†

N. P. Mayr<sup>1,\*</sup>, A. Hapfelmeier<sup>2</sup>, K. Martin<sup>3</sup>, A. Kurz<sup>2</sup>, P. van der Starre<sup>4</sup>, B. Babik<sup>5</sup>, D. Mazzitelli<sup>6</sup>, R. Lange<sup>6</sup>, G. Wiesner<sup>1</sup> and P. Tassani-Prell<sup>1</sup>

British Journal of Anaesthesia, 116 (1): 90-9 (2016)

doi: 10.1093/bja/aeu294

- INSERT Trial – single center, balanced randomization
- Transfemoral Medtronic CoreValve™ in 66 patients
- Evaluated cerebral desaturations in sedation vs GA - NIRS
- Secondary look at neurocognitive outcomes

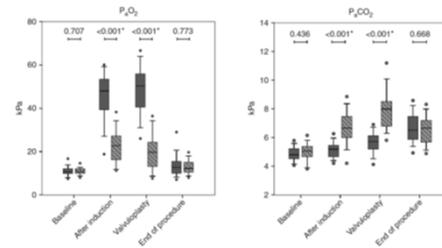
## Anesthetic plan

- TAVI-GA
  - Oral midazolam
  - Propofol 3mg/kg/hr (50 mcg/kg/min)
  - Remifentanyl 0.2 mcg/kg/min
- TAVI-S
  - Oral midazolam
  - Propofol 1 mg/kg/hr (16.7 mcg/kg/min)
  - Remifentanyl 0.03 mcg/kg/min

## Results

	TAVI-GA n=31	TAVI-S n=31	P-value
<b>rSO<sub>2</sub> values</b>			
rSO <sub>2</sub> at room air baseline (%)	60 (5/36)	57 (5/67)	0.916
rSO <sub>2</sub> interhemispheric difference (%)	0 (-3/3)	0 (-5/3)	0.789
rSO <sub>2</sub> with oxygen after induction (%)	65 (24/70)	68 (33/78)	<0.111
rSO <sub>2</sub> before RVP (%)	68 (6/71)	70 (6/79)	0.107
rSO <sub>2</sub> minimal value during RVP (%)	58 (5/164)	60 (5/67)	0.323
rSO <sub>2</sub> before valve implantation (%)	68 (58/72)	69 (64/78)	0.161
rSO <sub>2</sub> minimal value during valve impl. (%)	60 (5/166)	62 (5/71)	0.430
rSO <sub>2</sub> 120 S after extubation (%)	73 (62/78)	72 (66/79)	0.921
<b>Adverse events</b>			
Oversed/Plab n (%)	0	19 (61)	<0.001*
Bradypnea n (%)	n.a.	16 (52)	n.a.
SpO <sub>2</sub> <95% n (%)	0	5 (16)	0.028
low Transcatheter/aerway n (%)	n.a.	11 (36)	n.a.
Bag Mask Ventilation n (%)	n.a.	6 (19)	n.a.
Difficult tracheal intubation n (%)	3 (10)	n.a.	n.a.
Bronchospasm n (%)	0	1 (3)	1.000
Difficult central venous catheter n (%)	1 (3)	3 (10)	0.612
Defibrillation n (%)	0	1 (3)	1.000
Perioperative Stroke n (%)	0	1 (3)	1.000
Cumulative no. of patients with adverse events n (%)	4 (13)	29 (94)	<0.001*

## Blood Gas Analysis



## Discussion

- No statistical difference in cerebral desaturation
- No differences in neurocognitive testing
- High rate of adverse events
  - Primarily respiratory ~ 20% required BMV
  - Hypercarbia/respiratory acidosis – during procedure
  - Hypoxia
- No obvious safety concerns related to anesthetic choice

## Monitored Anesthesia Care Versus General Anesthesia: Experience With the Medtronic CoreValve



Christopher Palermo, DO, MPH,<sup>1</sup> Meredith Degnan, MD,<sup>2</sup> Keith Candiotti, MD,<sup>1</sup> Tomas Salerno, MD,<sup>1</sup> Eduardo de Marchena, MD,<sup>1</sup> and Yilam Rodriguez-Blanco, MD<sup>1</sup>

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- Retrospective, case controlled study- single health system
- 65 patients undergoing TAVR with Medtronic CoreValve™
- GA (n=21) or MAC (n=44) was utilized
- Hospital LOS, morbidity and mortality data reviewed

## Anesthetic Plan

- MAC
  - Dexmedetomidine load: 1mcg/kg over 10-15 min
    - Infusion 0.2-0.7 mcg/kg/hr
  - Fentanyl 25 mcg bolus PRN
  - 1% lidocaine at catheter site
- GA
  - Etomidate 0.2-0.6 mg/kg
  - NMB
  - Sevoflurane

Table 2. Surgical Characteristics/Complications

	GA n = 21	MAC n = 44	p-value
Postop mean AV gradient	8.8 ± 4.3	11.6 ± 5.9	0.054
Procedure time	260.0 ± 56.5	256.1 ± 50.7	0.771
Conversion to open	0%	0%	N/A
Pulmonary embolism	9%	2%	0.183
Pneumonia	4%	0%	0.146
Congestive heart failure	0%	0%	N/A
CVA	0%	2%	0.480
Cardiac arrest	0%	0%	N/A
Intraoperative mortality	0%	0%	N/A
1-month mortality	0%	2%	0.488
Sepsis	0%	2%	0.488
Pericardial tamponade	0%	0%	N/A
ICU readmission	4%	0%	0.146
Coronary revascularization	0%	4%	0.321
Postoperative AKI	0%	9%	0.154
Postoperative permanent PCM	28%	36%	0.427
Hematoma	14%	9%	0.527
ICU stay (days)	3.8 ± 2.8	4.1 ± 4.2	0.473
Hospital stay (days)	5.7 ± 2.5	6.3 ± 3.7	0.514
Intraoperative PRBC	0.43 ± 1.0	0.09 ± 0.29	0.047
Intraoperative FFP	0.19 ± 0.6	0	0.028
Intraoperative cryoprecipitate	0	0	N/A
Intraoperative platelets	0.10 ± 0.4	0	0.149
Postoperative PRBC	0.24 ± 0.6	0.50 ± 1.0	0.286
Postoperative FFP	0	0	N/A
Postoperative cryoprecipitate	0	0	N/A
Postoperative platelets	0	0	N/A

\*NOTE: Values are for percentage for listed techniques, mean ± SD.

## Conclusions

- No significant outcomes differences
- Underpowered to detect significant differences
- During learning curve phase of institution
- Comorbid CAD more likely to get GA
  - Also more likely to get transfusions
- No risks or benefits between anesthetic choice

## New Devices coming to you

- Atrial Fibrillation Occlusion devices
- Only 30-50% of Atrial fibrillation patients treated with AC
  - 5 fold increased risk of CVA with Afib
  - AC reduces risk only 60% with 1-3% increased bleeding
  - Left Atrial Appendage – site of thrombus in 90% in AF
- Left Atrial Appendage Occlusion Devices
  - Catheter based delivery system with self expanding occluder
  - Trans-septal Puncture required

## WATCHMAN Device

- Boston Scientific, Marlborough, MA
- Only device with FDA approval in the US
- Central Nickel-titanium with 10 fixation anchors
- European Society of Cardiology Guidelines
  - 2012 - Class IIb (LOE B) recommendation for patients at high risk of stroke but contraindication to AC
- Indications for AC currently based on CHA<sub>2</sub>DS<sub>2</sub>-VASc



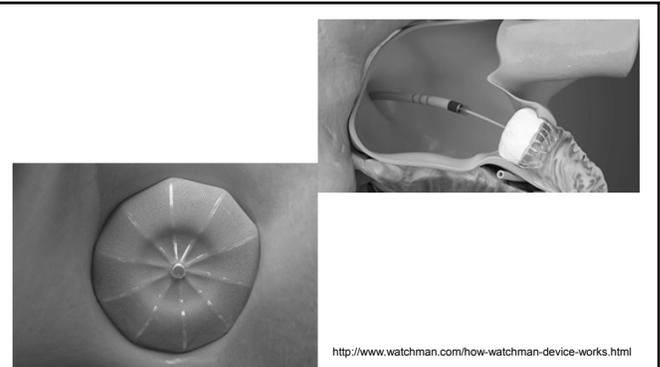
## Contraindications

- Presence of ASD or PFO closure device
- Inability to tolerate warfarin, ASA, or clopidogrel
  - ASA/warfarin used for 45 days post procedure
  - 45 d – 6 mo: ASA/clopidogrel
  - 6 mo+ ASA Monotherapy
  - Endocarditis prophylaxis initial 6 mos

## Outcomes Data

- PROTECT AF
  - Efficacy endpoint of stroke, CV death, embolic event
    - 2.3/100 vs 3.8/100 events compared to warfarin
- PREVAIL
  - Endpoint of ischemic stroke prevention
    - Non-inferior to warfarin therapy

Homes DR Jr. J Am Coll Cardiol 64:1-12, 2014  
Fountain RB Am Heart J 151:956-961, 2006.



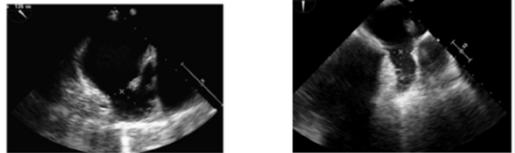
<http://www.watchman.com/how-watchman-device-works.html>

## TEE guided procedure

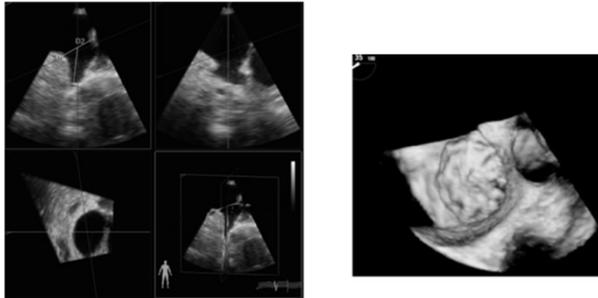
- Identify contraindications to procedure
- Aid fluoro guided direction of device
- Identify size, morphology, # of lobes relative to ostium
- Rapid recognition of procedural complications
  - Pericardial effusions

## TEE Assessment

- LAA measured ostium, depth
  - ME 4C: 0-20°, 45-60°, ME 2C: 90°, ME LAX: 120-135°
- 0° and 135° may show largest ostial diameter



*Journal of Cardiothoracic and Vascular Anesthesia, Vol 30, No 6 (December), 2016; pp 1685-1692*



## Atrial Fibrillation

- 20-50% incidence post cardiac surgery
- Increased rates of
  - Death
  - Complications
  - Cost of hospitalization
- Non-surgical Patients: AFFIRM trial\*
  - No advantage to rhythm control vs rate control

\*NEJM 2002;347:1825-33.

## The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

MAY 19, 2016

VOL. 374 NO. 20

### Rate Control versus Rhythm Control for Atrial Fibrillation after Cardiac Surgery

A.M. Gillinov, E. Bajbouj, A.J. Mackinnon, J.M. Rastan, M.A. Groh, M.E. Bowditch, G. Alami, S.A. Kikano, L.P. Perrault, M.E. Parides, R.L. Smith, E.J.A. Sims, G. Dussanik, S.E. Fischman, N.O. Jefferson, M.A. Miller, W.C. Tabbal-Peters, E.A. Rose, R.D. Weisel, D.L. Williams, R.F. Mangano, M. Argenteano, E.G. Moquete, K.L. O'Sullivan, M. Hebert, K.J. Shah, J.S. Gammie, M.L. Mazer, P. Vassine, A.C. Gelino, P.T. O'Garra, and M.J. Mack, for the CTSN\*

- Cardiothoracic Surgical Trials Network (CTSN), 23 sites
- CABG, Valve repair, bioprosthetic valve replacement
- 2109 patients enrolled
- 695 (33%) developed atrial fibrillation

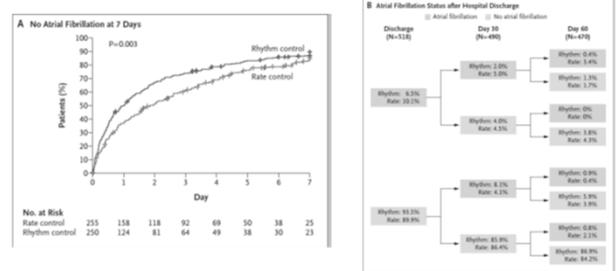
## Methodology

- Rate Control Group (n=255)
  - Medications to control HR <100
  - Could be converted if provider thought necessary for hemodynamics or symptoms
- Rhythm Control (n=250)
  - Amiodarone +/- rate controls agents for 24-48 hrs
  - DCCV recommended at that time for failure to convert
  - Amiodarone continued for 60 days unless side effects
- Pts DC'ed home in rate control or after amio load

## Outcomes

- Primary
  - Total hospital days within 60 days of randomization
- Secondary
  - Days to DC from randomization
  - Need for readmission
  - Need for PPM
  - Other adverse events

## Atrial Fibrillation Results



## Discussion

- 10x size of previous trials
- ~25% non-adherence to trial outline
  - Multiple crossovers reflecting clinical practice
- No primary end point differences – hospital days
  - Readmission rate still 28% - 1/5 for Atrial Fib issues
- Rhythm control achieved more SR faster
- Overall in total study participants
  - 85% in SR by discharge
  - 95% by 6 mo

## Take Home Points

- No measurable differences
- Rate control avoids toxic side effects of amio
  - At a cost of slower onset to rhythm control
    - More Anti-coagulation
- Most deviations from rhythm control group were amio toxicity side effects
- Continue to practice clinical bedside medicine

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

### Effect of Short-Term vs. Long-Term Blood Storage on Mortality after Transfusion

N.M. Heddle, R.J. Cook, D.M. Arnold, Y. Liu, R. Barty, M.A. Crowther, P.J. Devereaux, J. Hirsh, T.E. Warkentin, K.E. Weber, D. Roxby, M. Soberaj-Teague, A. Kurz, D.I. Sessler, P. Figueroa, M. Ellis, and J.W. Eikelboom

N ENGL J MED 375:20 NEJM.ORG NOVEMBER 17, 2016

- INFORM trial
- All hospitalized patients receiving RBC transfusion
- Patients randomized to receive freshest vs oldest unit in blood bank
- Blood type A or O only in primary analysis, all types in secondary
- 24,736 patients studied at 6 institutions

## Results

- Circulatory d/o, trauma, neoplasm, GI bleed
  - 67% of all patients
- Average of 2 units RBC per patient
- Mortality 9.1% vs 8.7% in new vs old blood units
- Sub-group analysis of high risk patients with no difference
  - Includes CT surgery – 1 institution excluded

JAMA | Special Communication

## Clinical Practice Guidelines From the AABB Red Blood Cell Transfusion Thresholds and Storage

Jeffrey L. Carson, MD, Gordon Guyatt, MD, Nancy M. Heddle, MSc, Brenda J. Grossman, MD, MPH, Claudia S. Cohn, MD, PhD, Mark K. Fung, MD, PhD, Terry Gerritsma, MD, John B. Holcomb, MD, Lewis J. Kaplan, MD, Louis M. Katz, MD, Nikki Peterson, BA, Glenn Ramsey, MD, Sunil V. Rao, MD, John D. Roback, MD, PhD, Anyeh Shander, MD, Aaron A. R. Tobias, MD, PhD

JAMA. 2016;316(19):2025-2035. doi:10.1001/jama.2016.5185  
Published online October 12, 2016.

- Literature review to establish guidelines on blood transfusion
- Reviewed transfusion threshold and storage age guidelines
- RBC transfusion threshold – 31 RCTs
- RBC transfusion storage – 13 RCTs

## Practice Guidelines

- Recommendation 1
  - Threshold of 7 g/dL for hospitalized adult patients
  - 8 g/dL for those undergoing orthopedic or cardiac surgery
    - Or those with pre-existing cardiac conditions
- Recommendation 2
  - Patients should receive any unit of RBC within standard issue dates
  - There is no benefit to fresher blood

## Future Research

### Transfusion Requirements in Cardiac Surgery III (TRICS-III)

This study is currently recruiting participants. (see Contacts and Locations)  
Verified December 2016 by St. Michael's Hospital, Toronto

Sponsor:  
St. Michael's Hospital, Toronto

Information provided by (Responsible Party):  
St. Michael's Hospital, Toronto

ClinicalTrials.gov Identifier:  
NCT02042898

First received: January 17, 2014  
Last updated: December 9, 2016  
Last verified: December 2016  
History of Changes

### Red Cell Storage Duration and Outcomes in Cardiac Surgery

This study is currently recruiting participants. (see Contacts and Locations)  
Verified January 2017 by The Cleveland Clinic

Sponsor:  
The Cleveland Clinic

Information provided by (Responsible Party):  
D Sessler, Outcomes Research Consortium

ClinicalTrials.gov Identifier:  
NCT00458783

First received: April 9, 2007  
Last updated: January 19, 2017  
Last verified: January 2017  
History of Changes

### Comparison of Two Different Red Blood Cell Transfusion Thresholds on Short-Term Clinical Outcomes of Patients Undergoing Aortic Surgery With Deep Hypothermic Circulatory Arrest

Yongyuan Wang, BA, and Hongwen Ji, MD

Journal of Cardiothoracic and Vascular Anesthesia, Vol 30, No 5 (October), 2016; pp 1163-1166

- Single center retrospective analysis
- 2 surgical teams with different thresholds for transfusion
  - Restrictive < 8 g/dL or Liberal < 10g/dL
- 74 patients studied over 1 year undergoing aortic surgery with DHCA

Table 4. Postoperative Mortality and Complications Compared Between the 2 Groups of Patients

Variable	Liberal Group (n = 38)	Restrictive Group (n = 40)	P Value
Re-exploration for bleeding, n (%)	1 (2.6%)	0	0.459
Need for dialysis, n (%)	4 (11.3%)	4 (10%)	1.000
Pulmonary infections, n (%)	5 (14.7%)	3 (7.5%)	0.468
Incision infection, n (%)	2 (5.9%)	0	0.208
Stroke, n (%)	0	2 (5%)	0.496
30-day mortality, n (%)	2 (5.9%)	3 (7.5%)	1.000
Duration of mechanical ventilation, h	36 ± 30	40 ± 39	0.077
ICU length of stay, h	100 ± 18	81 ± 10	0.464
Postoperative length of stay, days	11.9 ± 4.5	11.2 ± 5.4	0.575
6-h drainage volume, mL	304 ± 141	309 ± 215	0.391
24-h urine output, mL	741 ± 302	682 ± 458	0.081
24-h urine output, mL	4,481 ± 1,295	3,793 ± 1,247	0.044

Abbreviation: ICU, intensive care unit.

- No significant differences in M&M between groups
- Restrictive group did receive more PCC
- Limitations
  - Retrospective
  - Small sample size

Review

### Over 50 Years of Fibrinogen Concentrate

Rubens Costa-Filho, MD, FCCP<sup>1</sup>, Gerald Hochleitner<sup>2</sup>,  
Michael Wendt<sup>1</sup>, Alexandre Teruya, MD<sup>1</sup>, and  
Donat R. Spahn, MD, FRCA<sup>1</sup>

Clinical and Applied  
Thrombosis/Hemostasis  
2016, Vol. 22(2) 109-114 |

- The first license granted for fibrinogen concentrate was in Brazil in March 1963
  - Was available prior in unregulated forms
- 1985 – Pasteurization step added for viral inactivation
  - 3 million grams have been used since
  - Available as Haemocomplettan® or RiaSTAP® (US version)

## Fibrinogen Concentrate

- During major bleeding events, fibrinogen is the first clotting factor to reach critically low levels
- 1/23,300 cases of thrombotic events in post-marketing surveillance
- Purification of recombinant fibrinogen was completed in 1993
- Multiple clinical trials underway to investigate its use in major bleeding

## REPLACE Trial

Randomized evaluation of fibrinogen vs placebo in complex cardiovascular surgery (REPLACE): a double-blind phase III study of haemostatic therapy

N. Rahe-Meyer<sup>1,2</sup>, J. H. Levy<sup>3</sup>, C. D. Mazer<sup>4</sup>, A. Schramko<sup>4</sup>, A. A. Klein<sup>5</sup>, R. Brat<sup>6</sup>, Y. Okita<sup>7</sup>, Y. Ueda<sup>8</sup>, D. S. Schmidt<sup>9</sup>, R. Ranganath<sup>10</sup> and R. Gill<sup>11</sup>

*British Journal of Anaesthesia*, 117 (1): 41-51 (2016)

doi: 10.1093/bja/aew169

- Elective Aortic surgery randomized to fibrinogen concentrate (FCH) vs placebo

## Methodology

- Phase III, multinational, multi-center, randomized, double blinded trial in 2012-2014
- Post heparin reversal bleeding 60-250 g in 5 minutes
- FCH concentrates given to target FIBTEM maximal clot firmness (MCF) of 22mm
- Standard transfusion algorithm followed if bleeding continued
- 68% adherence rate in transfusion algorithm

## Methodology



- 519 patients randomized
  - 367 did not meet bleeding criteria
  - 152 treated with FCH or placebo

## Outcomes

- End Points: total allogenic units transfused in 24 hours
  - RBC, FFP, and platelets
- Secondary Endpoints
  - Individual unit types transfused
  - Need for reoperation
  - Mortality
  - Plasma fibrinogen (Clauss assay)
  - MCF – FIBTEM assay using ROTEM device

## Data

- Primary outcome
  - Increased RBC and FFP use with FCH
- Secondary outcomes
  - Increased fibrinogen levels and MCF target achieved
  - No differences in periop bleeding between groups
- Wide variability between centers

CARDIOVASCULAR

Preoperative supplementation with fibrinogen concentrate in cardiac surgery: A randomized controlled study

A. Jeppsson<sup>1,2,\*</sup>, K. Waldén<sup>3</sup>, C. Roman-Emanuel<sup>1</sup>, L. Thimour-Bergström<sup>1</sup> and M. Karlsson<sup>4</sup>

British Journal of Anaesthesia, 116 (2): 208-14 (2016)

doi: 10.1093/bja/aev367

- 304 assessed for eligibility
- 52 enrolled
- Double blind, randomized, placebo controlled trial
- Fibrinogen did not influence bleeding

Table 1 Haemostatic variables in the fibrinogen and placebo groups at five time points before, during and after CPB. Mean (SD). Key: CPB, cardiopulmonary bypass; APTT, activated partial thromboplastin time; INR, international normalized ratio. \*P<0.05, \*\*P<0.01, \*\*\*P<0.001 vs the placebo group at the same time-point.

	after induction of anaesthesia	After fibrinogen or placebo	30 min after CPB	1 h after CPB	24 h after CPB	P-value
Fibrinogen (g l <sup>-1</sup> )	2.8 (0.3)	3.1 (0.4)**	2.3 (0.4)*	2.3 (0.4)*	3.9 (0.7)**	Group 0.006
Placebo	2.7 (0.3)	2.8 (0.4)	2.0 (0.4)	2.0 (0.3)	3.5 (0.8)	Time<0.001
Haemoglobin (g l <sup>-1</sup> )	143 (27)**	135 (27)**	119 (23)	111 (23)	107 (23)	Group-Time 0.019
Placebo	131 (26)	123 (26)	103 (20)	104 (21)	107 (23)	Time<0.001
Platelet count (x10 <sup>9</sup> l <sup>-1</sup> )	215 (53)	215 (56)	156 (53)	170 (54)	184 (66)	Group-Time 0.17
Fibrinogen	195 (40)	189 (42)	144 (42)	162 (44)	171 (42)	Time<0.001
Placebo	195 (40)	189 (42)	144 (42)	162 (44)	171 (42)	Group-Time 0.25
APTT (s)	31.9 (2.5)	34.4 (2.4)	34.3 (3.3)	33.8 (2.7)*	35.5 (3.3)	Group-0.048
Fibrinogen	31.8 (2.4)	34.3 (2.3)	36.0 (4.4)	36.1 (3.6)	37.5 (4.7)	Time<0.001
Placebo	31.8 (2.4)	34.3 (2.3)	36.0 (4.4)	36.1 (3.6)	37.5 (4.7)	Group-Time 0.12
INR	1.09 (0.07)	1.12 (0.07)	1.02 (0.18)	1.06 (0.14)	1.05 (0.14)	Time<0.001
Fibrinogen	1.14 (0.13)	1.17 (0.13)	1.11 (0.13)	1.09 (0.13)	1.02 (0.20)	Group-Time 0.36
Placebo	1.14 (0.13)	1.17 (0.13)	1.11 (0.13)	1.09 (0.13)	1.02 (0.20)	Time<0.001

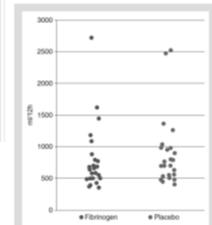


Fig 2 Postoperative blood loss volume in individual subjects. There was no significant difference in median volume between the fibrinogen and placebo groups, P=0.3.

Table 1 Bleeding and transfusions. Median (25th and 75th percentiles), mean (SD) or number (N)

	Fibrinogen (n=24)	Placebo (n=24)	P-value
Intraoperative blood loss (ml)			
Median	300 (200-400)	300 (200-500)	0.41
Mean	308 (210)	375 (290)	0.16
Postoperative blood loss (ml 12 h <sup>-1</sup> )			
Median	400 (300-500)	792 (243-960)	0.28
Mean	796 (523)	897 (553)	0.52
Total blood loss within 12 h (ml)			
Median	913 (615-1230)	1395 (950-1590)	0.18
Mean	1103 (518)	1272 (588)	0.30
Re-exploration for bleeding	1 (4.2%)	2 (8.4%)	0.55
Red blood cell transfusion			
Number of patients	4 (16.7%)	4 (16.7%)	1.00
Mean volume (units)	0.63 (0.17)	1.33 (1.13)	0.30
Median volume (units)	0 (0-0)	0 (0-0)	0.68
Plasma transfusion			
Number of patients	3 (12.5%)	6 (25.0%)	0.27
Mean volume (units)	0.25 (0.48)	0.58 (1.33)	0.19
Median volume (units)	0 (0-0)	0 (0-0)	0.45
Platelet transfusion			
Number of patients	2 (8.3%)	4 (16.7%)	0.38
Mean volume (units)	0.17 (0.48)	0.25 (0.70)	0.47
Median volume (units)	0 (0-0)	0 (0-0)	0.47
Area allogeneic transfusion			
Number of patients	8 (33.3%)	7 (29.2%)	0.76
Mean volume (units)	1.04 (2.11)	2.29 (4.47)	0.22
Median volume (units)	0 (0-0)	0 (0-3)	0.58

Efficacy and Safety of Fibrinogen Concentrate in Surgical Patients: A Meta-Analysis of Randomized Controlled Trials

Evgeny Fominisky, MD, PhD,<sup>1</sup> Valeriy A. Nepomniashchikh, MD, PhD,<sup>1</sup> Vladimir V. Lomivorotov, MD, PhD,<sup>1</sup> Fabrizio Monaco, MD,<sup>2</sup> Chiara Vitello, MD,<sup>2</sup> Alberto Zangrillo, MD,<sup>3</sup> and Giovanni Landoni, MD,<sup>4</sup>

Journal of Cardiothoracic and Vascular Anesthesia, Vol 30, No 5 (October), 2016; pp 1196-1204

Objectives: To investigate the efficacy and safety of fibrinogen concentrate (FC) in surgical patients.

Design: Meta-analysis of randomized controlled studies.

Setting: RCTs.

Participants: Adult and pediatric surgical patients.

Intervention: A search of PubMed/Medline, Embase, Cochrane Central Register of Controlled Trials, Translational Evidence Library, Google Scholar, and the proceedings from major international anesthesiology meetings, as well as references.

Measurements and Main Results: The primary outcome was all-cause mortality. Pooled risk ratios and mean differences (MDs) were compared with active bleed-effects or transfusion effects. The study included 14 RCTs comprising 1,028 patients, the majority of patients underwent cardiac surgery. All cause mortality was lower in the fibrinogen group (0.02, 95% CI -0.02, 0.03, risk ratio 0.50, 95% CI 0.04-0.78, p = 0.02; heterogeneity: I<sup>2</sup> = 0%). The use of FC was associated with reduced bleeding (MD -127 mL, 95% CI -207 to -47, p = 0.002, 95% CI) and a lower number of red blood cells transfused (mean comparison MD -8.8, 95% CI -1.3 to -6.3, p < 0.001, I<sup>2</sup> = 62%). There were no differences in the rates of thrombotic events and myocardial infarction.

Conclusions: In surgical patients, FC was associated with reduced bleeding and a lower number of red blood cells transfused, as well as a lower number of myocardial infarction. There was no difference in the rates of thrombotic events and myocardial infarction.

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KEY WORDS: surgery, anaesthesia, fibrinogen, efficacy, safety

Fig 2 Forest plot for all cause mortality. Mantel-Haenszel method (95% CI).

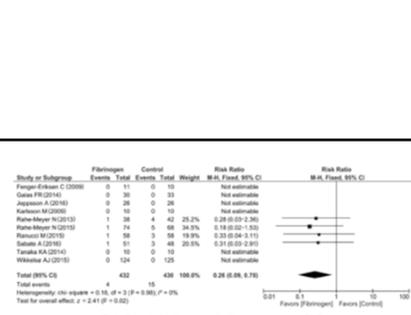
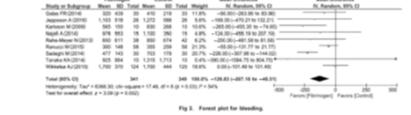


Fig 3 Forest plot for bleeding. Mantel-Haenszel method (95% CI).



Immediate postoperative extubation in bilateral lung transplantation: predictive factors and outcomes<sup>1</sup>

M.-L. Felten<sup>1,6</sup>, J.-D. Moyer<sup>1,6</sup>, J.-F. Dreyfus<sup>1,6</sup>, J.-Y. Marandon<sup>1,6</sup>, E. Sage<sup>3,6</sup>, A. Roux<sup>1,6</sup>, F. Parquin<sup>1,6</sup>, C. Cerf<sup>5</sup>, B. Zuber<sup>7</sup>, M. Le Guen<sup>1,6</sup> and M. Fischer<sup>1,6,\*</sup>, the Foch Lung Transplant Group

British Journal of Anaesthesia, 116 (6): 847-54 (2016)

doi: 10.1093/bja/aew119

- 89 Bilateral Lung Transplant (BLT) for patients with cystic fibrosis over 6 years
- Excluded pre-op ECMO, redo transplants, ex vivo lung reconditioning, and multiorgan transplants
- CPB was used if required

Table 1 Anaesthesia technique and local extubation guidelines. ECMO, extracorporeal membrane oxygenation;  $F_{iO_2}$ , fraction of inspired oxygen; ICU, intensive care unit; DNO, isoflurane; NO, nitric oxide; OR, operating room;  $P_{aO_2}$ , arterial partial pressure of oxygen;  $P_{aCO_2}$ , arterial partial pressure of carbon dioxide;  $P_{aO_2}/P_{aCO_2}$ , arterial partial pressure of oxygen to carbon dioxide ratio

Anaesthesia technique	Evaluation at the end of surgery	Evaluation at the end of the non-invasive ventilation attempt
Hot air warming blanket	Double-lumen tube changed to a single-lumen tube. Fiberoptic bronchoscopy	Success of the non-invasive ventilation attempt if the patient is well orientated, pain free, and with no clinical signs of acute respiratory distress, and if $P_{aO_2}/P_{aCO_2}$ ratio >26.6 kPa and $P_{aO_2}/P_{aCO_2}$ <6.7 kPa (arterial blood gas checked after 20 min) – patients transferred to ICU on a high-concentration oxygen face mask (E-OR group)
Epidual catheter levobupivacaine 0.125% and sufentanil 0.2 µg ml <sup>-1</sup> infusion at 1 ml h <sup>-1</sup>	Tidal volume of 6 ml kg <sup>-1</sup> , rate of ventilation according to $P_{aO_2}/P_{aCO_2}$ between 60 and 100% according to arterial oxygen saturation ( $P_{aO_2}$ )	Failure of the non-invasive ventilation attempt reintubation and transfer to ICU (E-OR group)
Neopropofol 1.2 µg kg <sup>-1</sup> min <sup>-1</sup>	Arterial blood gas analysis $P_{aO_2}/P_{aCO_2}$ <13.3–ECMO	
Propofol and remifentanyl according to the bispectral index (target range 40–60), anaesthetist for non-muscular block	$P_{aO_2}/P_{aCO_2}$ >13.3–40–continuation of mechanical ventilation; double-lumen tube positioned under bronchoscopic guidance	
Tidal volume of 6–8 ml kg <sup>-1</sup> during double-lung ventilation and 4 ml kg <sup>-1</sup> during one-lung ventilation; 15–20 breaths min <sup>-1</sup> ; $F_{iO_2}$ adjusted to arterial blood gas results; systematic N2O	$P_{aO_2}/P_{aCO_2}$ >16–extubation protocol if other requirements are fulfilled (no visible pulmonary oedema, no need for DNO; $P_{aO_2}/P_{aCO_2}$ <6.7 kPa; lactate <3 mmol l <sup>-1</sup> ; $SpO_2$ >95%; haemoglobin >10 g dl <sup>-1</sup> ; temperature >36°C; haemodynamic stability; low vasoactive drug needs; no coagulation issues; no significant bleeding seen in the chest tubes)	
Broad-spectrum antibiotics according to the recipient culture; immuno-suppression	No extubation in the OR in event of unfavourable evaluation (E-OR group)	
Routine monitoring, arterial catheter, oesophageal pulmonary arterial catheter (Bios-Gate CCM3Med) versus oxygen saturation ( $P_{aO_2}$ ) catheter, Edwards Lifesciences Corp., Irvine, CA, USA), bispectral index monitoring (Aspect A-2000 XE, version 3.11, Aspect Medical Systems, Ipswich, MA, USA), transoesophageal echocardiography (Vivid 7; GE Healthcare, Fairfield, CT, USA)	Extubation protocol in event of favourable evaluation: antagonism of non-muscular block, end of propofol and remifentanyl, semi-sitting position, extubation; non-invasive ventilation in the operating room for 20 min using a face mask and a Respronic ventilator (Philips Healthcare, The Netherlands) with bi-level positive airway pressure; respiratory and respiratory airway pressure of 8 and 4 cm H <sub>2</sub> O, respectively, with an $F_{iO_2}$ of 1	

Table 2 Intraoperative data. Data are expressed as numbers (percentage) or medians [25th–75th percentile] and are compared using Fisher's exact test or the Mann-Whitney U-test. ECMO, extracorporeal membrane oxygenation; E-OR, extubation in the intensive care unit; E-OR, extubation in the operating room; FFF, fresh frozen plasma; FFO, red blood cells

	E-OR group (n=41)	E-OR group (n=48)	P-value
Thrombotic episodes (n (%))	36 (88.0)	37 (77.1)	0.08
Anaesthetic induction complications (n (%))	4 (9.7)	4 (8.3)	0.75
Anaesthetic maintenance complications before intubation (n (%))	9 (21.9)	12 (25.0)	0.82
First graft			
Ventilation complications (n (%))	9 (21.9)	19 (39.6)	0.11
Pulmonary artery cross-clamping complications (n (%))	11 (26.8)	20 (41.7)	0.36
Pulmonary artery unclamping complications (n (%))	10 (24.4)	15 (31.3)	0.49
Ischaemic time (min)	240 (142.5–290.0)	246 (171.7–291.5)	0.34
Ventilation complications (n (%))	3 (7.3)	21 (43.8)	<0.001
Pulmonary artery cross-clamping complications (n (%))	4 (9.7)	19 (39.6)	0.001
Pulmonary artery unclamping complications (n (%))	9 (21.9)	18 (37.5)	0.17
Ischaemic time (min)	346 (261.5–392.5)	366 (303.2–431.5)	0.17
Ventilation complications (n (%))	3 (7.3)	13 (27.1)	<0.001
ECMO (n (%))	7 (17.1)	20 (41.7)	0.02
RBC use (kg l <sup>-1</sup> )	30 (115.5–24.5)	26 (101.6–36.5)	0.04
FFF (ml kg <sup>-1</sup> )	38 (105–27.5)	21 (115.9–31.5)	0.23
Colloid (ml kg <sup>-1</sup> )	30 (115.5–36.5)	35 (144.4–47.5)	0.05
Cryoprecipitate (ml kg <sup>-1</sup> )	26 (115.5–26.5)	27 (104.4–34.5)	0.90
Platelets (million platelets l <sup>-1</sup> )	3 (7)	12 (25)	0.04
Lactarase (mmol l <sup>-1</sup> )	2.1 (1.4–3)	2.4 (1.83–3.4)	0.03