UNIKLINIK KÖLN
Department of Cardiothoracic Surgery
University Hospital of Cologne

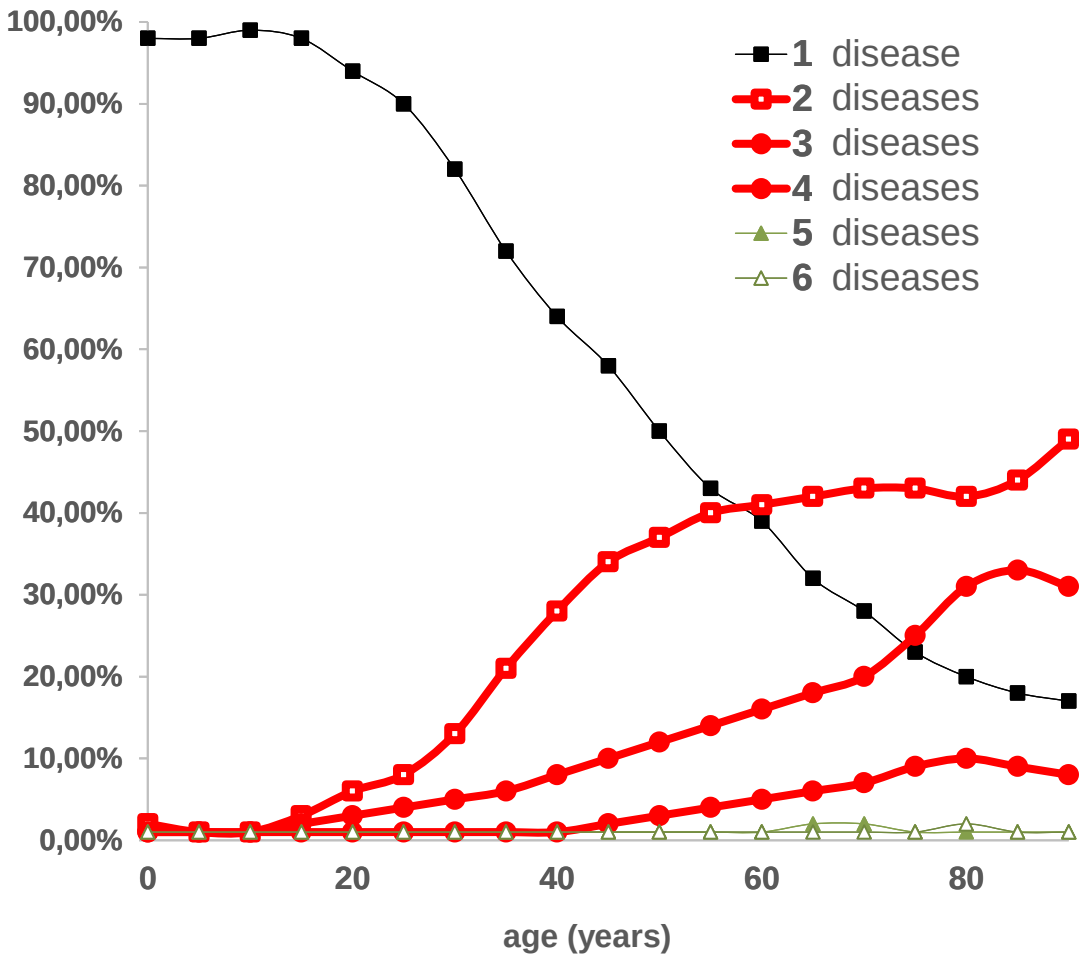
- Athens 9-11 June 2016 -

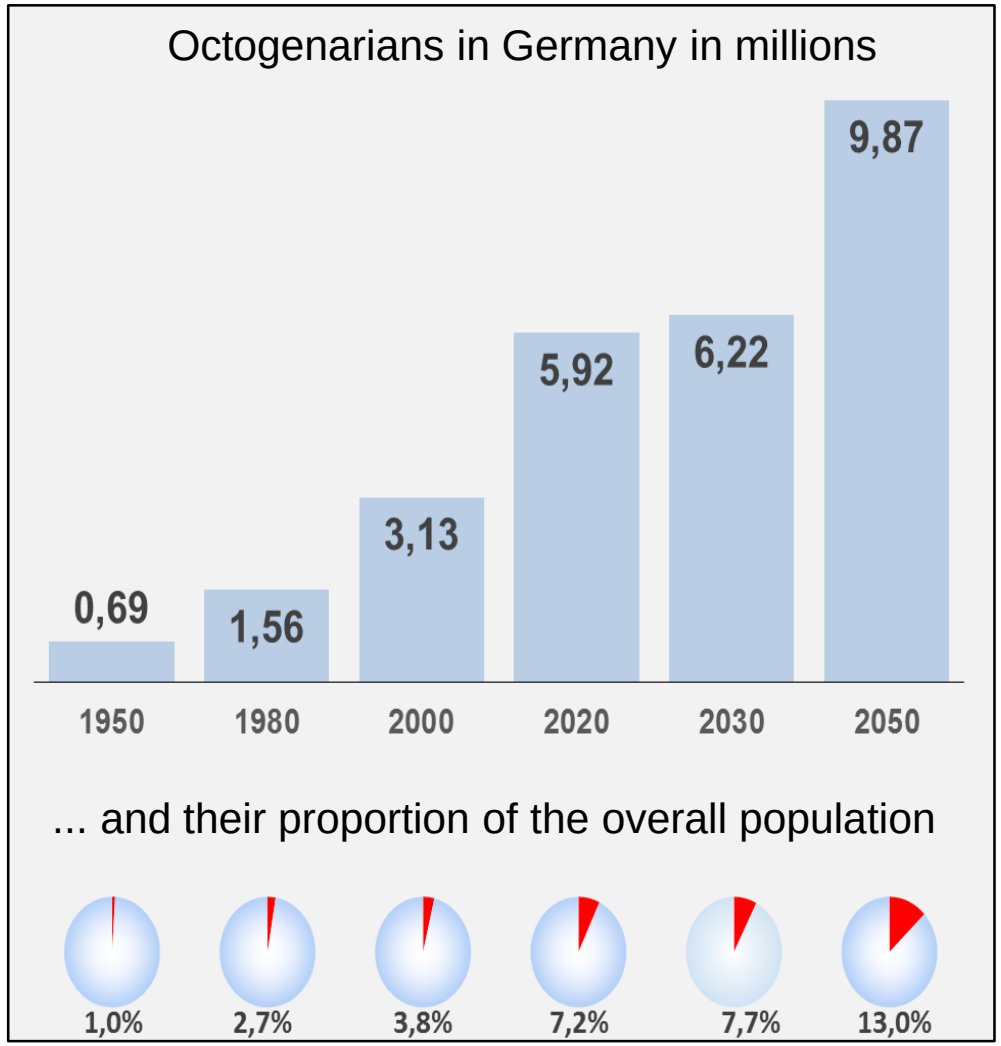
MiECT 2nd International Symposium on Minimal Invasive Extracorporeal Technologies

Conventional ECC versus MiECC: Current Scientific Evidence

Oliver J. Liakopoulos, MD, PhD

Multimorbidity of the Elderly



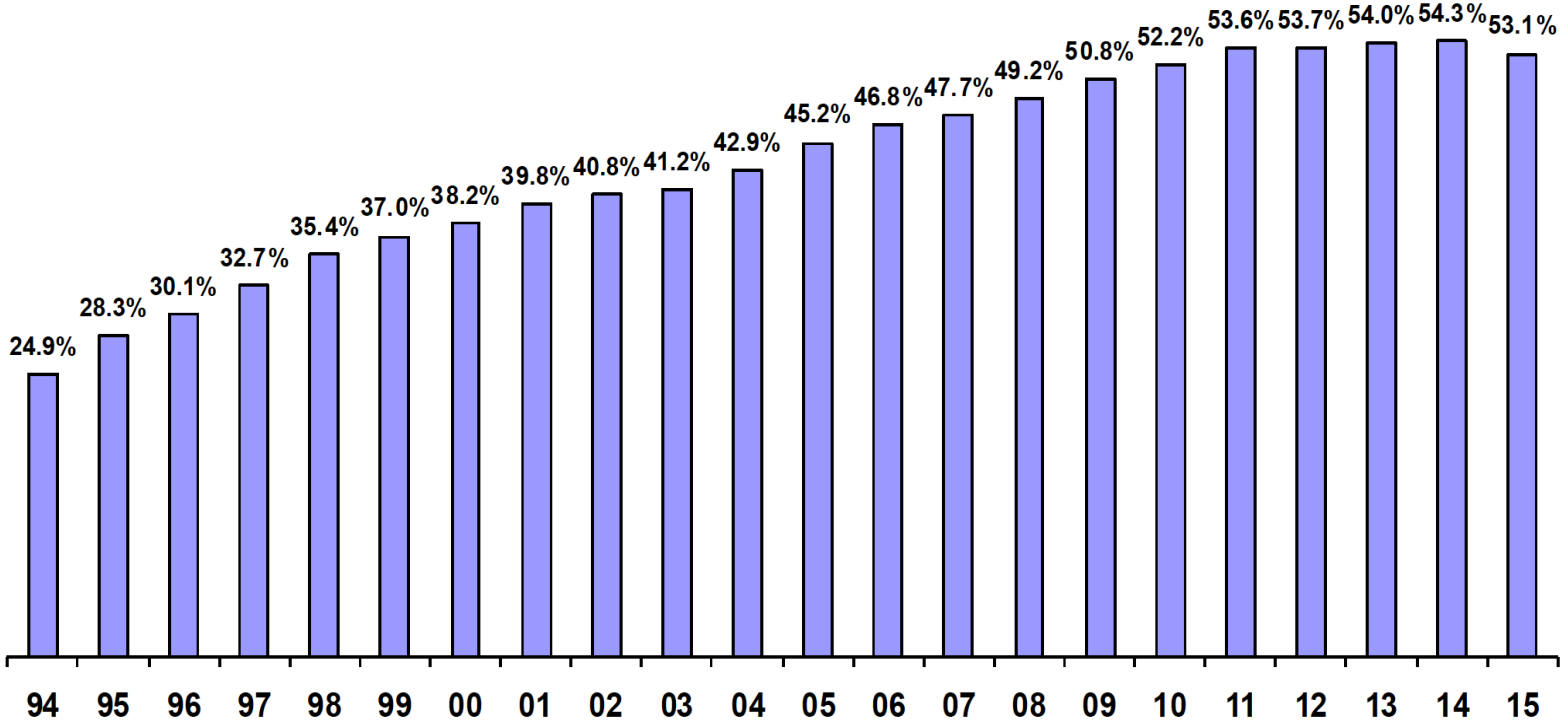


The Boston Consulting Group, 2015

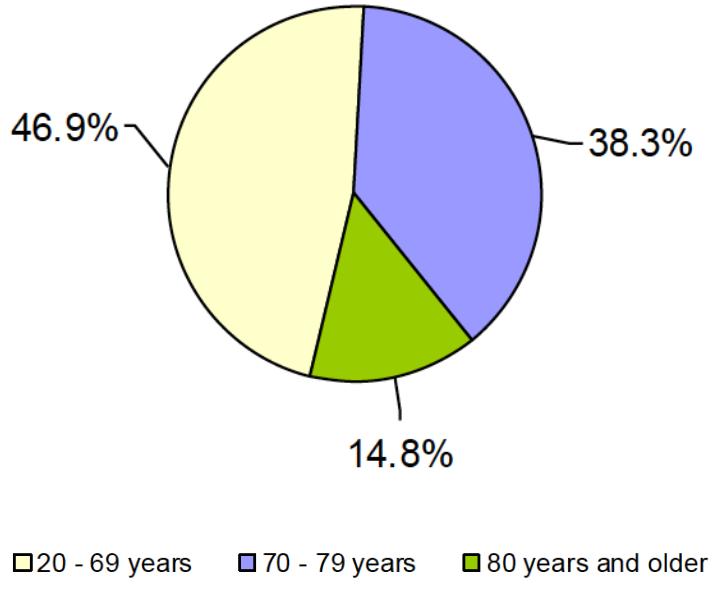
Age of Patients - 1994-2015

Annual Report 2016 - German Society Of thoracic and Cardiovascular Surgery

Patients 70 years and older

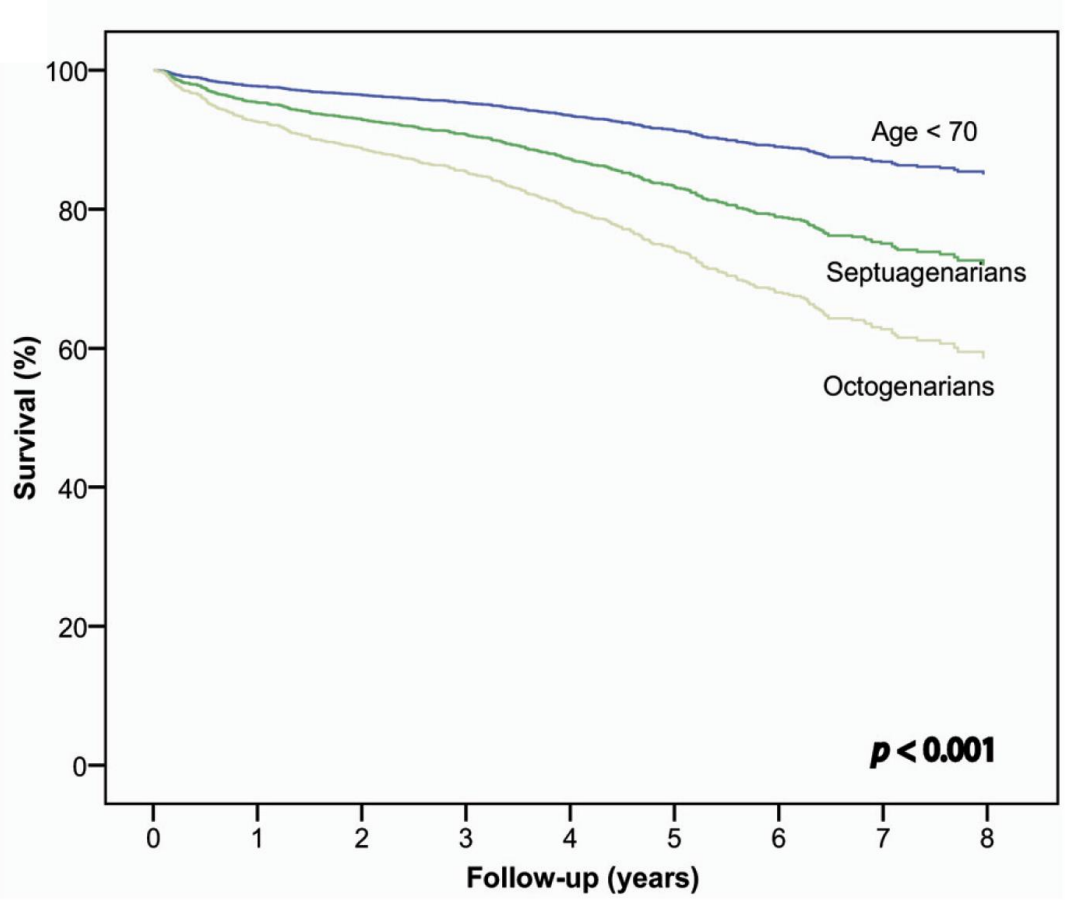


Age distribution 2015



Outcome of the Elderly after Cardiac Surgery

Adjusted Survival after CABG



Filsufi et al., J Cardiothorac Vasc Anesth 2007

Predictors for in-hospital mortality

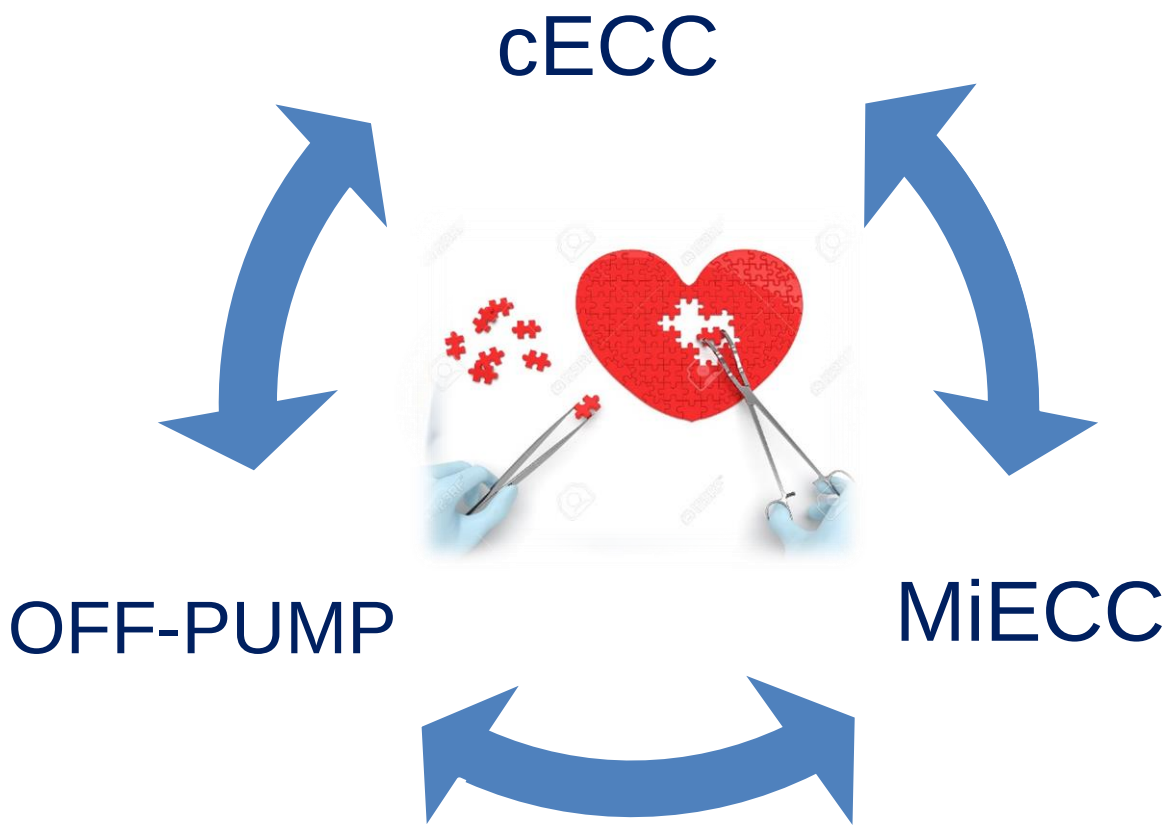
Multivariate analysis of preoperative and intraoperative variables associated with in-hospital mortality among patients 80 years old and older undergoing isolated coronary artery bypass grafting

Predictor	β Estimate	SE	χ^2	*P* value*	Odds ratio	95% Confidence interval
Preoperative						
Date of surgery	−0.0002	.0001	7.54	.006	1.0	1.0–1.0
Arrhythmia	0.6809	.2289	8.52	.004	2.0	1.3–3.1
Abnormal ejection fraction	0.6228	.2494	6.61	.010	1.9	1.1–3.0
Renal insufficiency (creatinine ≥2.0 mg/dL)	0.9048	.2581	11.26	.001	2.5	1.5–4.1
Nonelective surgical urgency	0.6010	.2406	5.93	.015	1.8	1.1–2.9
Intraoperative						
Conduit (saphenous vein)	0.5448	.2554	4.73	.030	1.7	1.0–2.8
Perfusion time	0.0117	.0044	6.50	.011	1.0	1.0–1.0

∗ Only significant differences ($P < .05$) are listed.

Kurlansky et al. J Thorac Cardiovasc Surg 2011

Strategies for Patients at High Risk



MiECC vs conventional ECC

Proposed benefits of MiECC

Closed, miniaturized circuit

Reduced priming volume

Heparin coating

No blood-to-air interaction

No cardiotomy suction

Centrifugal pump

No venous reservoir

SIRS

Blood activation

Coagulation

Microembolization

Hemodilution

Mechanical trauma

Does MiECC limit cECC related morbidity and mortality ?

MiECC vs. cECC

Less blood transfusions

Panday GF, Fischer S, Bauer A, et al. Minimal extracorporeal circulation and off-pump compared to conventional cardiopulmonary bypass in coronary surgery. Interact Cardiovasc Thorac Surg 2009;9:832-6.

Reduced systemic inflammation

Anastasiadis K, Antonitsis P, Haidich AB, et al. Use of minimal extracorporeal circulation improves outcome after heart surgery; a systematic review and meta-analysis of randomized controlled trials. Int J Cardiol 2013;164:158-69.

Reduced myocardial injury

Anastasiadis K, Antonitsis P, Haidich AB, Argiriadou H, Deliopoulos A, Papakonstantinou C. Use of minimal extracorporeal circulation improves outcome after heart surgery; a systematic review and meta-analysis of randomized controlled trials. Int J Cardiol 2013;164:158-69.

Significant less circulating endothelial cells

Skrabal CA, Choi YH, Kaminski A, et al. Circulating endothelial cells demonstrate an attenuation of endothelial damage by minimizing the extracorporeal circulation. J Thorac Cardiovasc Surg 2006;132:291-6.

Significantly lower incidence of postoperative AKIN and cerebral events

Benedetto U, Luciani R, Goracci M, et al. Miniaturized cardiopulmonary bypass and acute kidney injury in coronary artery bypass graft surgery. Ann Thorac Surg 2009;88:529-35.

Biancari F, Rimpiläinen R. Meta-Analysis of RCTs comparing the effectiveness of miniaturised versus conventional CPB in adult cardiac surgery. Heart 2009:95:964-9.

Significantly reduced mortality

Anastasiadis K, Antonitsis P, Haidich AB, Argiriadou H, Deliopoulos A, Papakonstantinou C. Use of minimal extracorporeal circulation improves outcome after heart surgery; a systematic review and meta-analysis of randomized controlled trials. Int J Cardiol 2013;164:158-69.

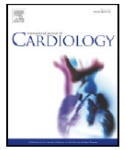
MiECC vs. cECC

International Journal of Cardiology 164 (2013) 158–169

Contents lists available at SciVerse ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard



Review

Use of minimal extracorporeal circulation improves outcome after heart surgery; a systematic review and meta-analysis of randomized controlled trials

Kyriakos Anastasiadis [a], Polychronis Antonitsis [a,*], Anna-Bettina Haidich [b], Helena Argiriadou [a], Apostolos Deliopoulos [a], Christos Papakonstantinou [a]

[a] Department of Cardiothoracic Surgery, Aristotle University of Thessaloniki, AHEPA Hospital, Thessaloniki, Greece
[b] Department of Medical Statistics, Laboratory of Hygiene, Medical School, Aristotle University of Thessaloniki, Greece

Systematic review of 24 RCTs (until 2010)

MiECC (n=1387) vs. Conventional ECC (n=1383)

Primary endpoints: Operative mortality, MI, stroke

Secondary endpoints

Subgroups: CABG (n=2049) and AVR (n=721)

	CABG			AVR		
	MiECC	cECC		MiECC	cECC	
Mortality	0.6%	1.9%	p=0.03	0.5%	0.9%	p=0.57
Myocardial Infarction	1.2%	4.2%	p=0.04	0.0%	1.7%	p=0.50
Stroke	2.3%	4.0%	p=0.08 *	*for both CABG and AVR		

...and less: Troponin, atrial fibrillation, LOS, RBC transfusions, Elastase levels, renal failure, ICU stay

MiECC vs. cECC

International Journal of Cardiology 198 (2015) 63–65

Contents lists available at ScienceDirect

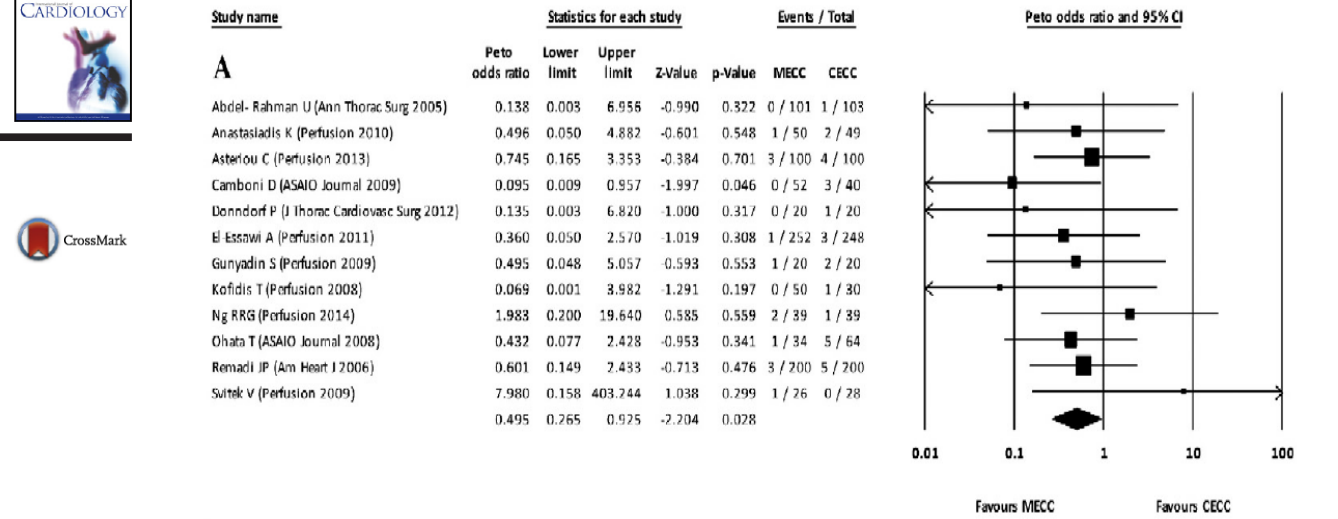
International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Letter to the Editor

30-day mortality reduction with miniaturized extracorporeal circulation as compared to conventional cardiopulmonary bypass for coronary revascularization. Meta-analysis of randomized controlled trials

Mariusz Kowalewski [a,b,e,*], Wojciech Pawliszak [a], Michalina Kołodziejczak [c,e], Eliano Pio Navarese [d,e], Lech Anisimowicz [a]



Study name	Peto odds ratio	Lower limit	Upper limit	Z-Value	p-Value	Events / Total MECC	Events / Total CECC
A							
Abdel- Rahman U (Ann Thorac Surg 2005)	0.138	0.008	6.956	-0.990	0.322	0 / 101	1 / 103
Anastasiadis K (Perfusion 2010)	0.496	0.050	4.882	-0.601	0.548	1 / 50	2 / 49
Asteriou C (Perfusion 2013)	0.745	0.165	3.353	-0.384	0.701	3 / 100	4 / 100
Camboni D (ASAIO Journal 2009)	0.095	0.009	0.957	-1.997	0.046	0 / 52	3 / 40
Donndorf P (J Thorac Cardiovasc Surg 2012)	0.135	0.003	6.820	-1.000	0.317	0 / 20	1 / 20
El-Essawi A (Perfusion 2011)	0.360	0.050	2.570	-1.019	0.308	1 / 252	3 / 248
Gunyadin S (Perfusion 2009)	0.495	0.048	5.057	-0.593	0.553	1 / 20	2 / 20
Kofidis T (Perfusion 2008)	0.069	0.001	3.982	-1.291	0.197	0 / 50	1 / 30
Ng RRG (Perfusion 2014)	1.983	0.200	19.640	0.585	0.559	2 / 39	1 / 39
Ohata T (ASAIO Journal 2008)	0.432	0.077	2.428	-0.953	0.341	1 / 34	5 / 64
Remadi JP (Am Heart J 2006)	0.601	0.149	2.433	-0.713	0.476	3 / 200	5 / 200
Svitek V (Perfusion 2009)	7.980	0.158	403.244	1.038	0.299	1 / 26	0 / 28
	0.495	0.265	0.925	-2.204	0.028		

Model	Number Studies	Point estimate	Lower limit	Upper limit	Z-value	P-value
Fixed	12	0.495	0.265	0.925	-2.204	0.028
Random	12	0.495	0.265	0.925	-2.204	0.028

Model — Effect size and 95% interval — Test of null (2-Tail)

Systematic review of 12 RCTs (until 2014?)

Only CABG

MiECC (n=944) vs. Conventional ECC (n=941)

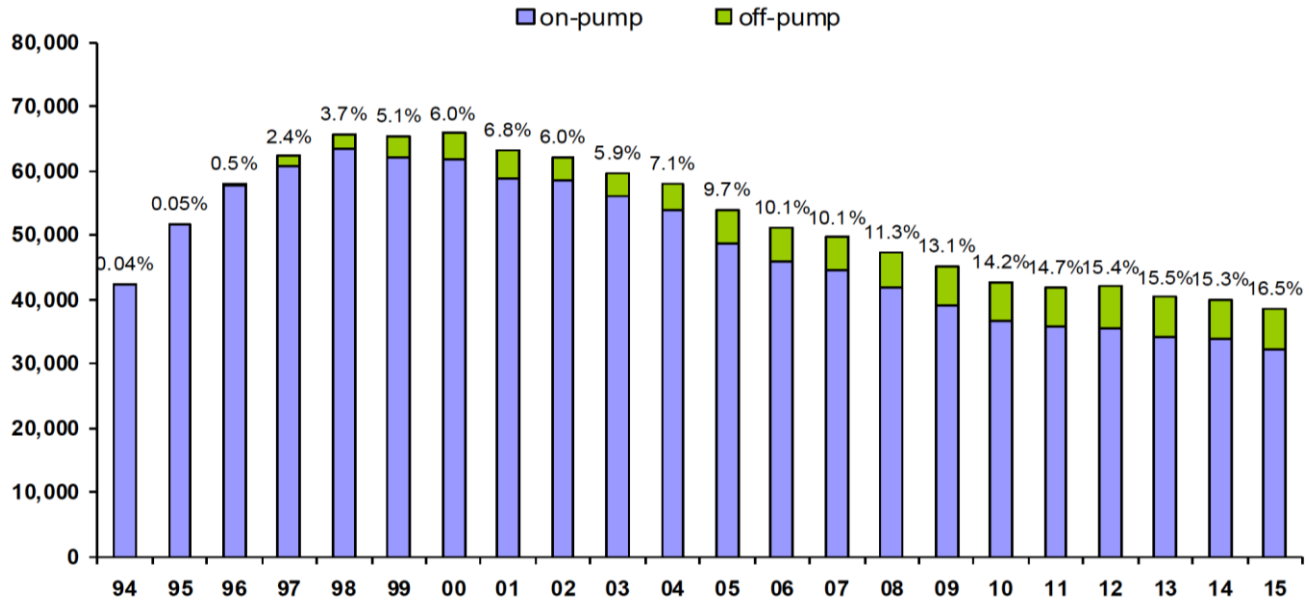
Primary endpoints: 30-day mortality

50% reduction of the odds of 30-day mortality !?

MiECC vs. Off-pump CABG

2014 ESC/EACTS Guidelines on myocardial revascularization

	Class	Level
Minimization of aortic manipulation is recommended.	I	B
Off-pump CABG should be considered for subgroups of high-risk patients in high-volume off-pump centres.	IIa	B
Off-pump CABG and/or no-touch on-pump techniques on the ascending aorta are recommended in patients with significant atherosclerotic disease of the ascending aorta in order to prevent perioperative stroke.	I	B



ANNUAL REPORT 2016 - GERMAN SOCIETY OF THORACIC AND CARDIOVASCULAR SURGERY

MiECC vs. OPCAB

Superior in terms of completeness of coronary revascularization

Panday GF, Fischer S, Bauer A, et al. Minimal extracorporeal circulation and off-pump compared to conventional cardiopulmonary bypass in coronary surgery. Interact Cardiovasc Thorac Surg 2009;9:832-6.

Mazzei V, Nasso G, Salamone G et al. Prospective Randomized Comparison of Coronary Bypass Grafting With Minimal Extracorporeal Circulation System. Circulation. 2007;116:1761-1767.

Comparable postoperative morbidity

Mazzei V, Nasso G, Salamone G et al. Prospective Randomized Comparison of Coronary Bypass Grafting With Minimal Extracorporeal Circulation System. Circulation. 2007;116:1761-1767.

Comparable inflammation

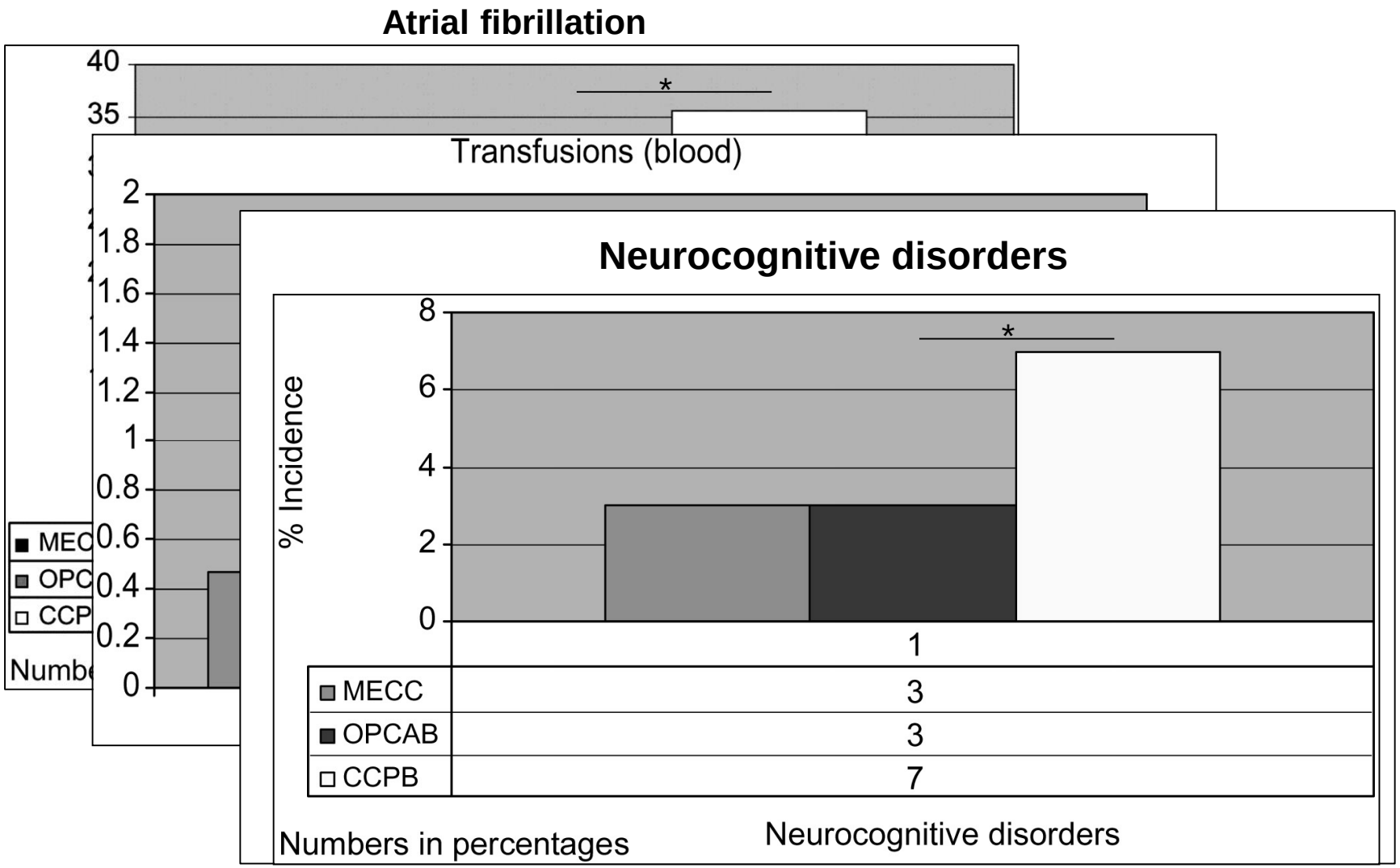
Mazzei V, Nasso G, Salamone G et al. Prospective Randomized Comparison of Coronary Bypass Grafting With Minimal Extracorporeal Circulation System. Circulation. 2007;116:1761-1767.

Formica F, Mariani S, Broccolo F et al. Systemic and myocardial inflammatory response incoronary artery bypass graft surgery with miniaturized extracorporeal circulation: differences with a standard circuit and off-pump technique in a randomized clinical trial. ASAIO J. 2013 Nov-Dec;59(6):600-6

Comparable low mortality

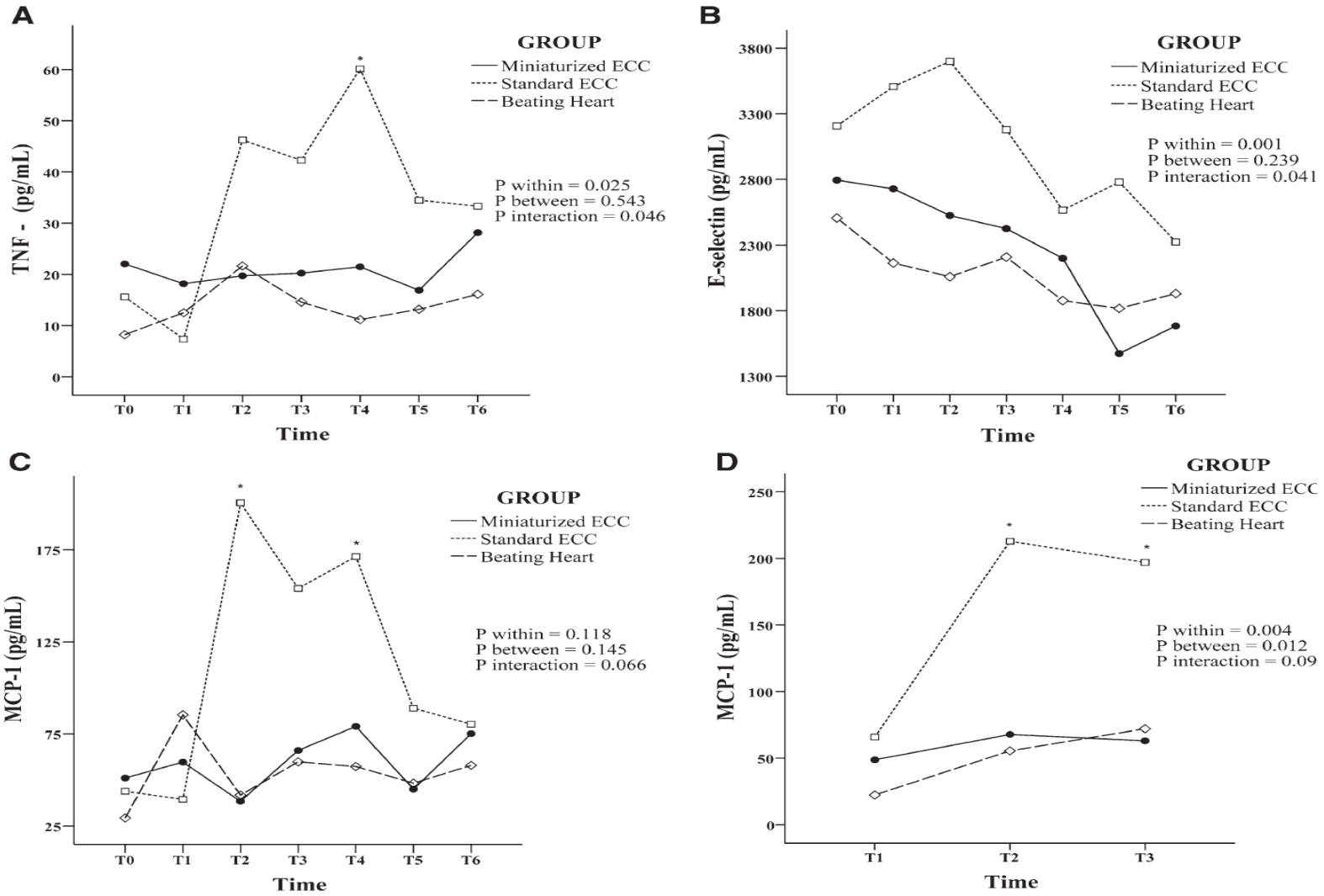
Anastasiadis K, Antonitsis P, Haidich AB, Argiriadou H, Deliopoulos A, Papakonstantinou C. Use of minimal extracorporeal circulation improves outcome after heart surgery; a systematic review and meta-analysis of randomized controlled trials. Int J Cardiol 2013;164:158-69.

MiECC vs. cECC vs. OPCAB



Panday, Interact CardioVasc Thorac Surg, 2009

MiECC vs. cECC vs. OPCAB



Formica et al. ASAIO J 2013

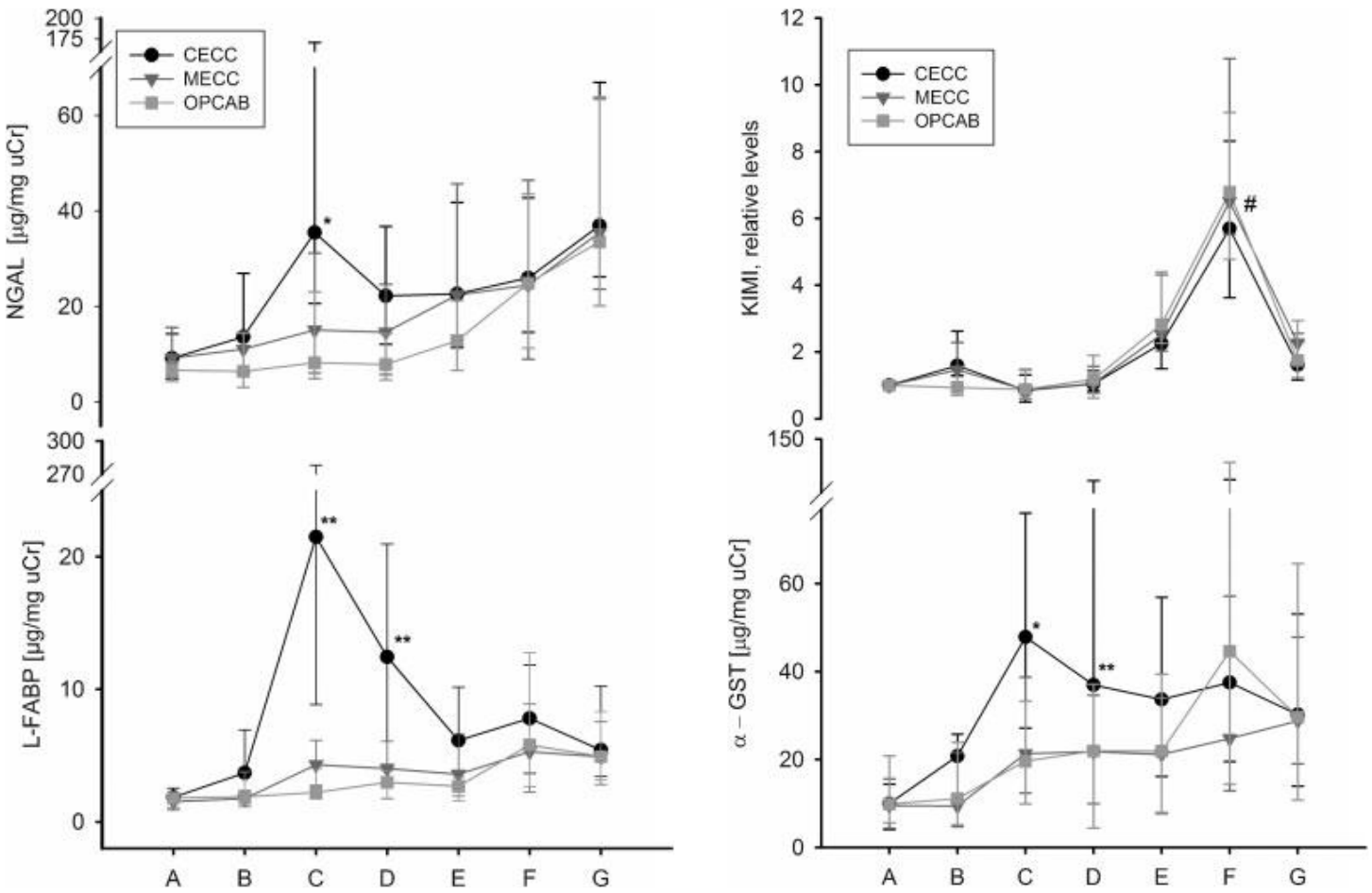
Conclusion:

MiECC is comparable to cECC and OPCAB in the clinical outcome of low-risk patients, and it might be extensively used with no additional intraoperative risk. The analysis of the inflammatory patterns of endothelial activation shows MiECC as effective as OPCAB, suggesting further studies to clarify MiECC recommendation in high-risk patients.

MiECC vs. cECC vs. OPCAB

Renal Function and Urinary Biomarkers in Cardiac Bypass Surgery: A Prospective Randomized Trial Comparing Three Surgical Techniques

Stefanie Deininger, Markus Hoenicka, Kristina Müller-Eising, Patricia Rupp, Andreas Liebold, Wolfgang Koenig, Hagen Gorki



NGAL
neutrophil gelatinase-associated lipocalin

KIM-1
kidney injury molecule-1

α-GST
α glutathione S-transferase

L-FABP
liver fatty acid-binding protein

Conclusion: During coronary artery bypass grafting, **cECC temporarily induces more tubular injury** than MiECC or OPCAB. However, late changes of renal function parameters occur irrespective of extracorporeal perfusion mode and even in off-pump surgery.

Thorac Cardiovasc Surg. 2015

Conclusive Evidence

Interactive CardioVascular and Thoracic Surgery 22 (2016) 647–662
doi:10.1093/icvts/ivv380 Advance Access publication 26 January 2016

INTERACTIVE CARDIOVASCULAR AND THORACIC SURGERY

Use of minimal invasive extracorporeal circulation in cardiac surgery: principles, definitions and potential benefits. A position paper from the Minimal invasive Extra-Corporeal Technologies international Society

Table 4: Summary of evidence-based practice guidelines

Recommendation	Level of evidence	References
Class I		
MiECC systems reduce haemodilution and better preserve haematocrit as well as reduce postoperative bleeding and the need for RBC transfusion	A	[17, 19, 20]
MiECC systems reduce the incidence of postoperative atrial fibrillation	A	[13, 16, 19, 20]
MiECC systems preserve renal function	A	[20, 39]
MiECC is associated with improved myocardial protection	A	[20, 43–45]
Class IIA		
Inflammatory response assessed by specific inflammatory markers is attenuated with use of MiECC	B	[23–26]
MiECC systems can reduce cerebral gaseous microembolism and preserve neurocognitive function	B	[20, 29–33]
MiECC exerts a subclinical protective effect on end-organ function (lung, liver, intestine) which is related to enhanced recovery of microvascular organ perfusion	B	[39, 46–48]
Class IIB		
Within a MiECC strategy, less thrombin generation may permit reduced heparin dose targeted to shorter ACT times. When such a strategy is followed, individual heparin dose should be determined using heparin dose–response monitoring systems	B	[14, 15, 56, 57]
MiECC appears to offer survival benefit in terms of lower 30-day mortality after CABG procedures	B	[20, 49, 50, 51]
The use of short-acting opioids in combination with propofol or volatile anaesthetics, and hypnotic effect monitoring by processed EEG, is recommended for induction and maintenance of anaesthesia for MiECC-based surgery. TOE findings pertinent to institutional management of MiECC should be communicated during the preoperative surgical safety time out	C	[16, 58–61]

Word of Caution !

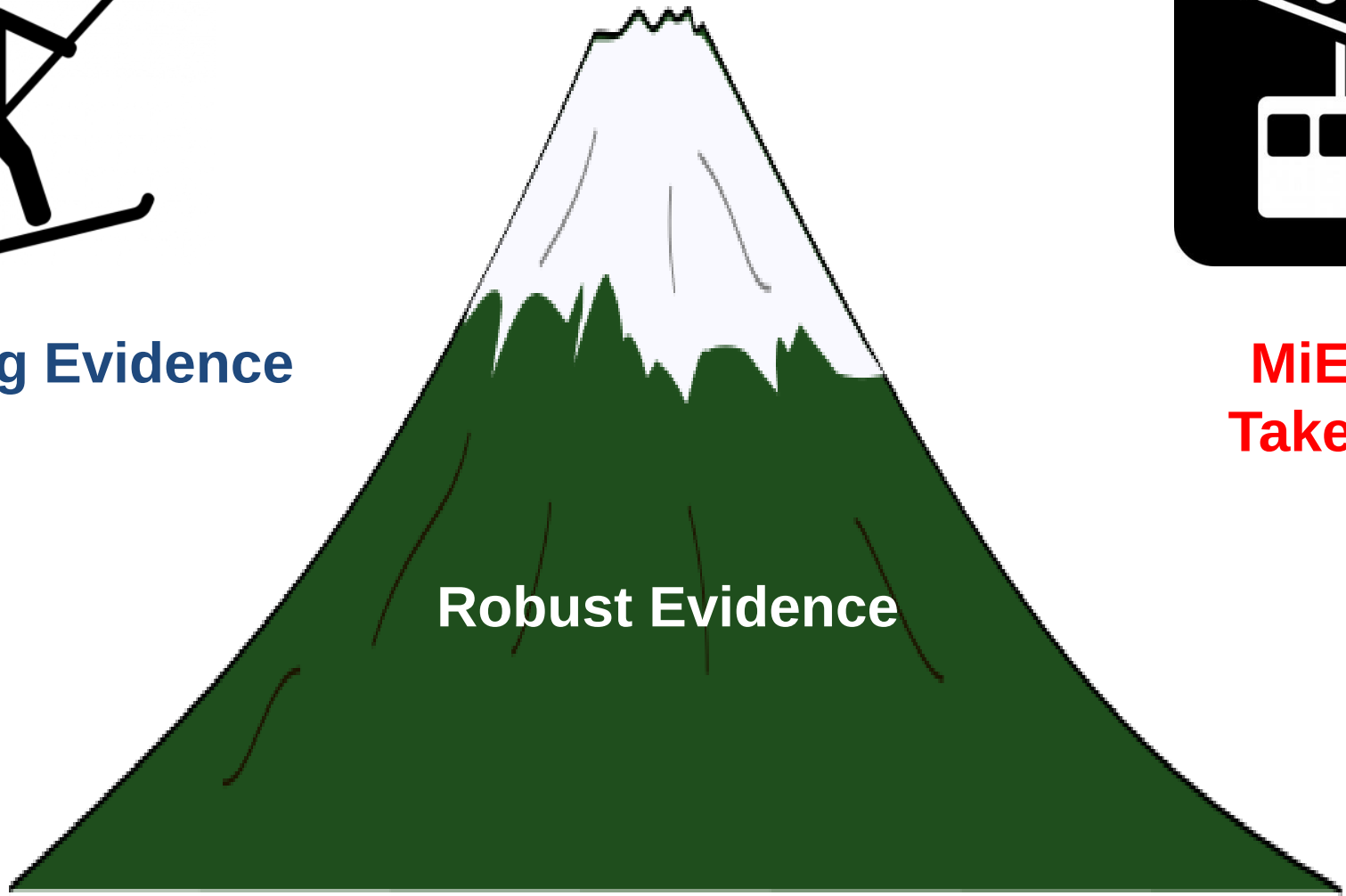
Existing evidence is predominatly based on small randomized controlled trials and pooled data analysis in systematic reviews

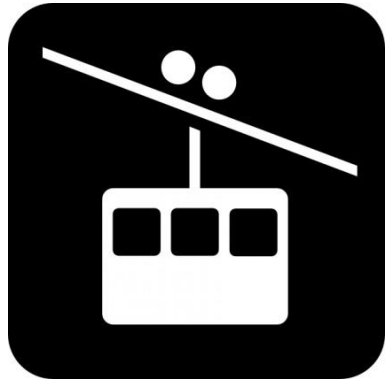
- Overestimation of treatment effect sizes
- Heterogenous setups with various MiECC protocols
- Unclear methods of treatment allocation
- Lack of power for clinical relevant endpoints
- Non-uniform definitions of clear clinical endpoints
- Monocentric design with limited external validity

COMICS Trial

Multicentre RCT

Building Evidence



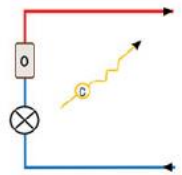
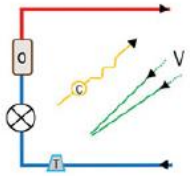
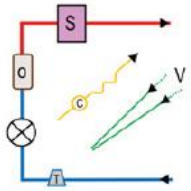
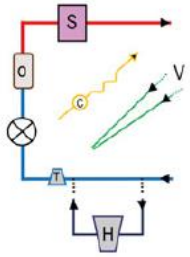


MiECC
Take-Off

Priv.-Doz. Dr. Oliver J. Liakopoulos

Heart Center of Cologne
Dept. of Cardiothoracic Surgery
Email: oliver.liakopoulos@uk-koeln.de

MiECC Systems - Classifications

Type I		Standard	This closed circuit comprises of an afferent tube (blue line) which drains blood from the right atrium to the pump (⊗), then to the oxygenator (O) and returns it to the arterial circulation with the efferent tube (red line). The oblique arrow indicates cardiopledgia line with its pump (©).
Type II		Air handling	A venous bubble trap/air removing device (T)is added to the standard MiECC circuit so as to facilitate air handling and avoid air entrainment to the venous line. Venting (green) lines (V) drain blood from the aortic root and/or pulmonary artery/vein.
Type III		Volume management	A soft shell reservoir (S) is added to the circuit to collect blood volume from the patient and return it back during perfusion according to the needs.
Type IV		Blood management	A hard shell reservoir (H) is added as an extra component integrated to the venous line, so as to convert the system to an open circuit that could facilitate blood management as well as overcome any other intraoperative issue (modular configuration).

Standard miniaturized CPB

per definition from here: MiECC

+ venous bubble trap

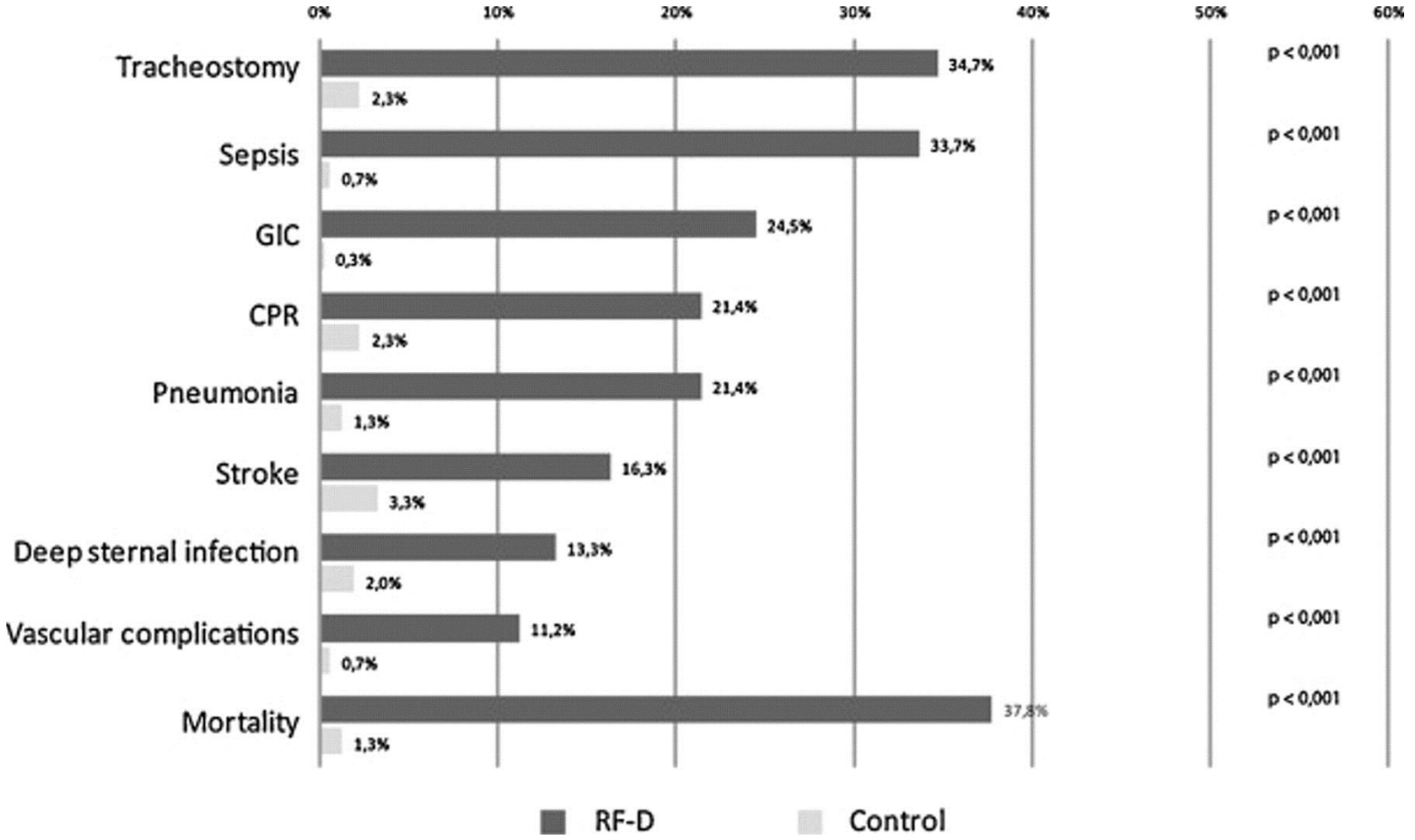
+ soft shell reservoir

+ hard shell reservoir
Modular system

Figure 1: Classification of MiECC circuits [12]. [Note that the modular type IV circuit is literally type III with a standing-by component, used only when necessary] (X: pump; O: oxygenator; C: cardioplegia; T: bubble trap/air-removing device; V: vent (aortic/pulmonary); S: soft-bag/reservoir; H: hard-shell/reservoir). MiECC: minimal invasive extracorporeal circulation.

Dialysis-Impact on Outcome

Mortality and morbidities stratified by the occurrence of RF-D, N = 2511



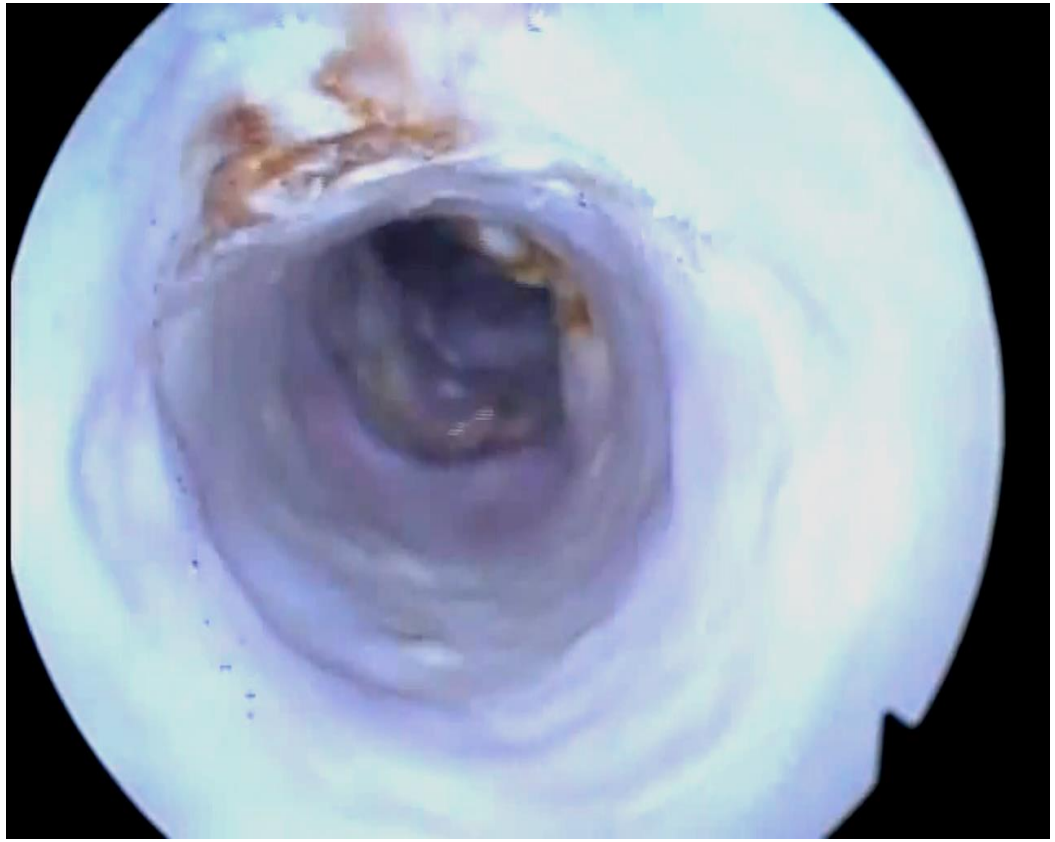
Rahmanian et al., Eur J Cardiothorac Surg, 2010

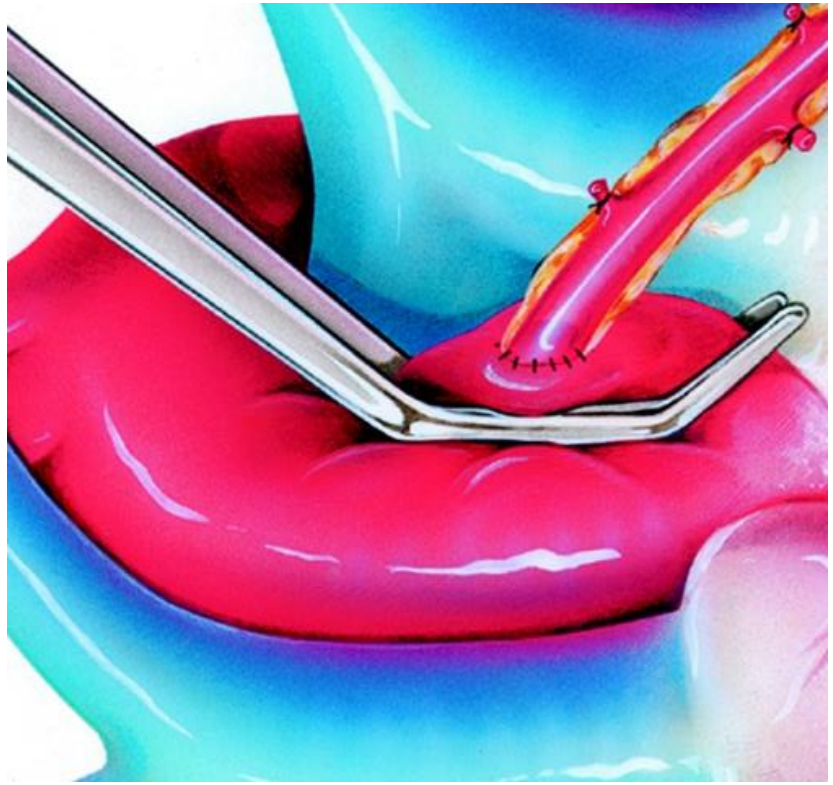
Beating Heart vs. OPCAB

Conclusions—Clinical results of coronary revascularization with MECC are optimal when this procedure is performed by experienced teams. Postoperative morbidity is comparable to that with OPCABG. MECC is associated with little pump-related systemic and organ injury. It may achieve the benefits of OPCABG (less morbidity in high-risk patients) while facilitating complete revascularization in the case of complex lesions unsuitable for OPCABG.

N = 538, Interact Cardiovasc Thorac Surg 2016

C-Clamp Effect

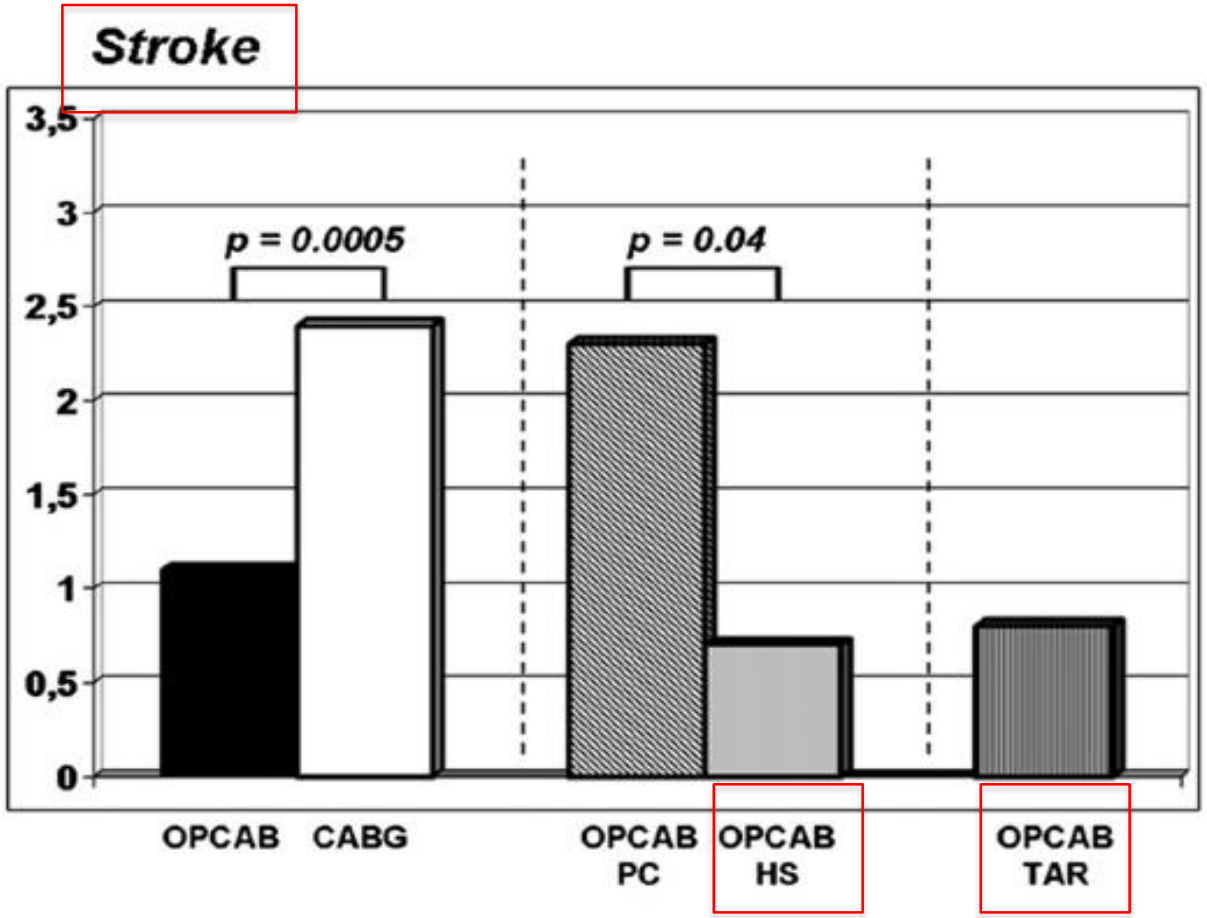


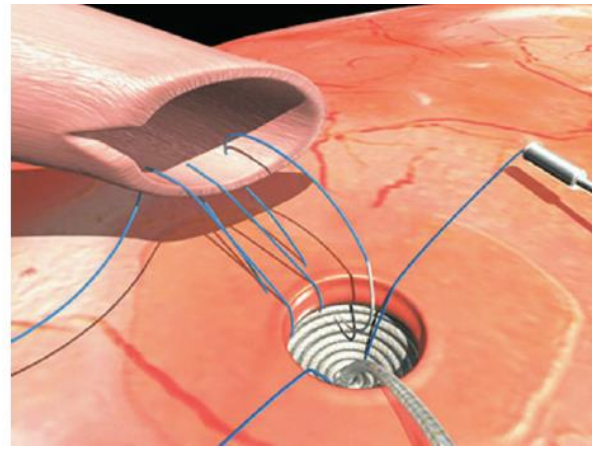


Courtesy of M. Emmert, Zurich

Minimal Aortic Manipulation

Aortic no-touch technique makes the difference in off-pump coronary bypass grafting
Emmert M Y, Seifert B, Wilhelm W, et al.



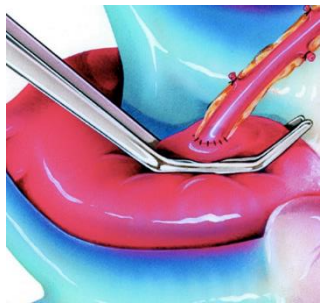


J Thorac Cardiovasc Surg 2012

Minimal Aortic Manipulation

Gaseous and solid cerebral microembolization during proximal aortic anastomoses in off-pump coronary surgery: The effect of an aortic side-biting clamp and two clampless devices

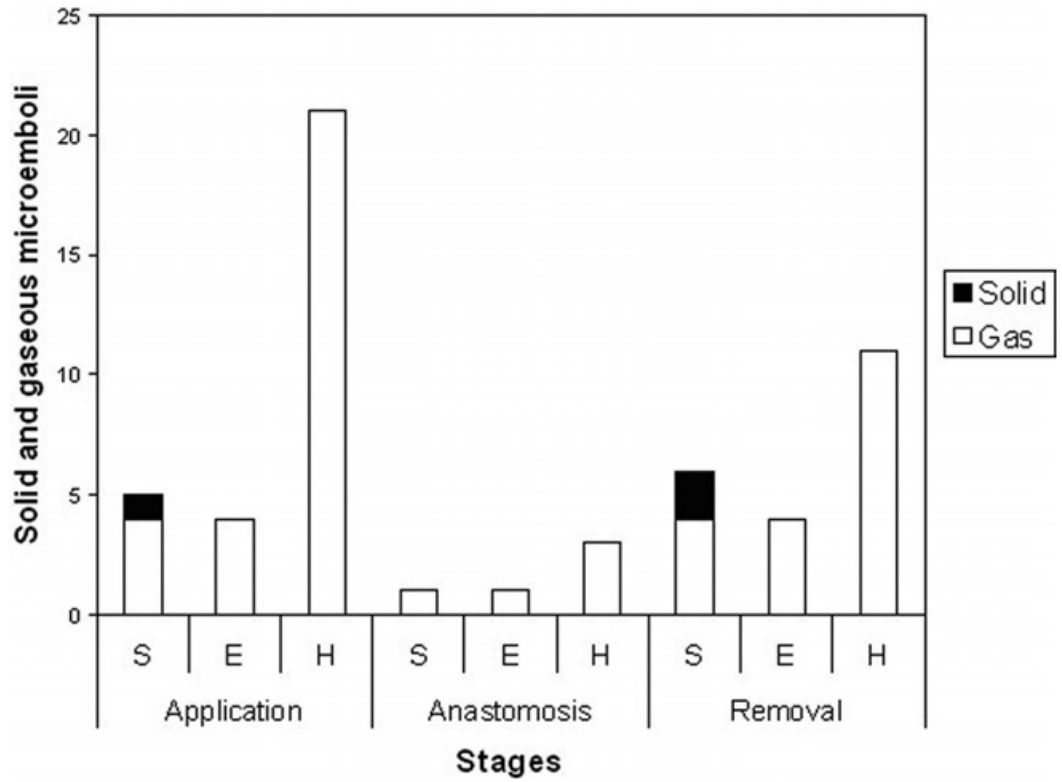
Lorenzo Guerrieri Wolf, MD, Yasir Abu-Omar, MRCS, Bikram P. Choudhary, MRCS, David Pigott, FRCA, and David P. Taggart, MD (Hons), PhD, FRCS



Side-bite

Enclose II

Heart String



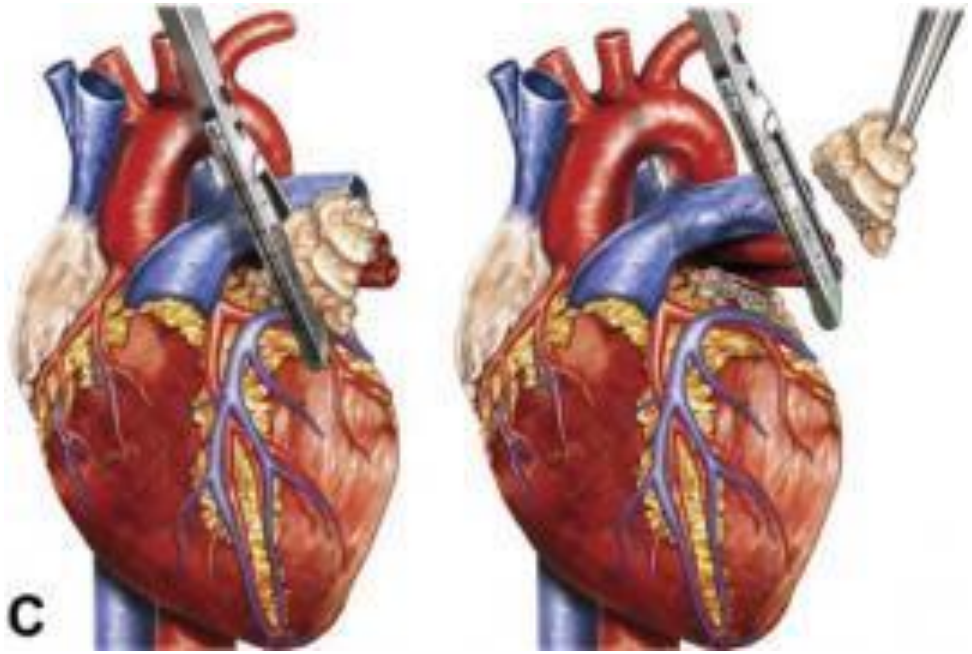
S, Side-biting clamp; E, Enclose; H, Heartstring

CONCLUSIONS

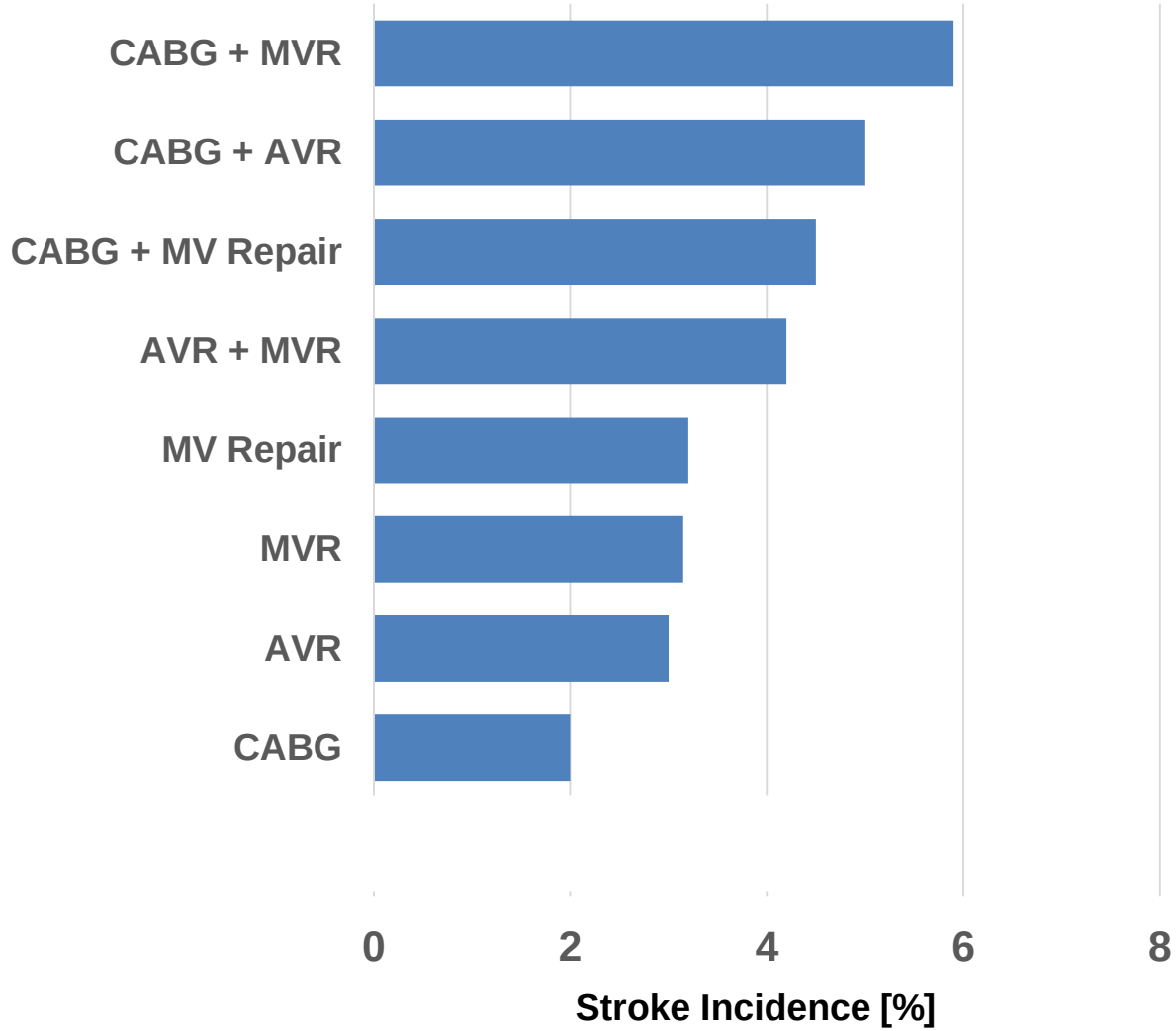
Avoidance of aortic side clamping results in a significant reduction in the proportion of solid microemboli detected with transcranial Doppler. As solid microemboli are probably the most damaging, use of the Enclose and Heartstring devices may represent an important strategy for minimizing cerebral injury during proximal aortic anastomoses.

J Thorac Cardiovasc Surg 2007

LAA Closure



Perioperative Stroke – Comparison



Courtesy of James Cox, US National Adult Cardiac Surgery Database, 2013

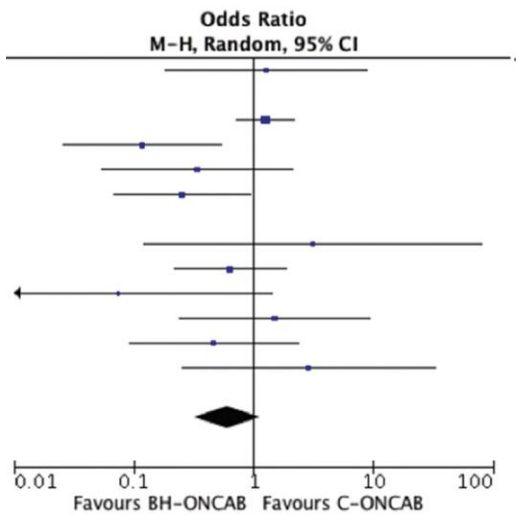
Beating Heart vs. CCPB

Beating-Heart Versus CCPB

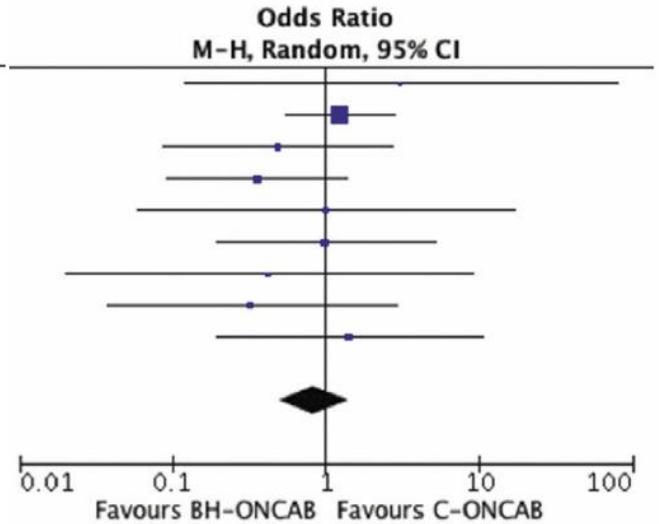
A Meta-Analysis of Clinical Outcomes

Umar A. R. Chaudhry, MBBS, Leanne Harling, MRCS, PhD, Amir H. Sepehripour, MRCS, George Stavridis, MD, John Kokotsakis, MD, Hutan Ashrafian, MRCS, PhD, and Thanos Athanasiou, FRCS, PhD

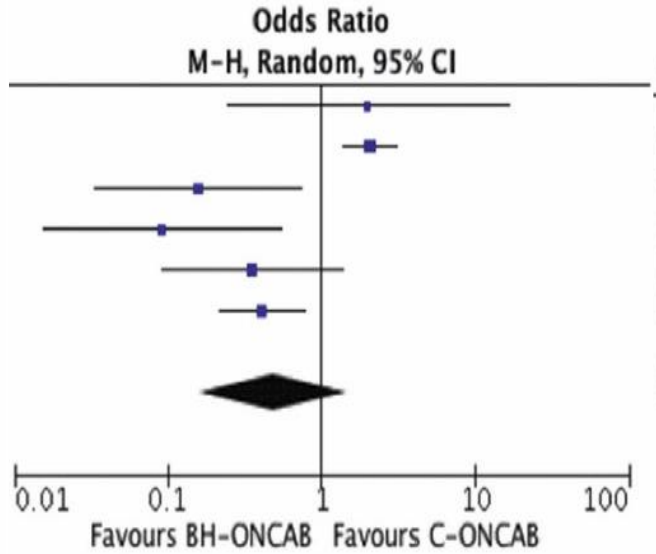
Mortality



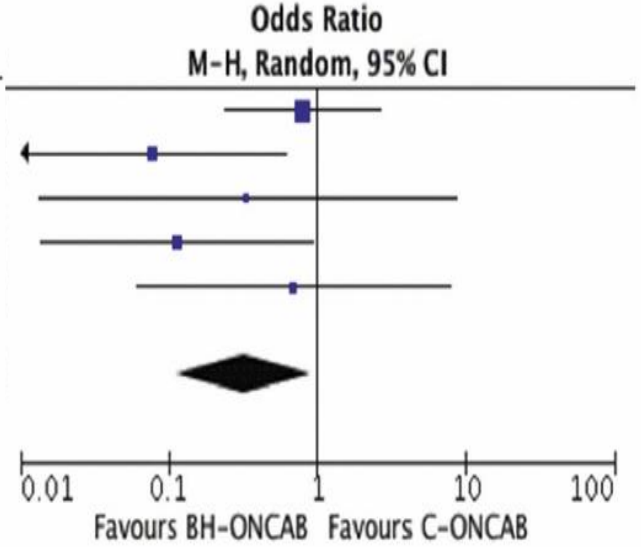
Stroke



Renal Failure

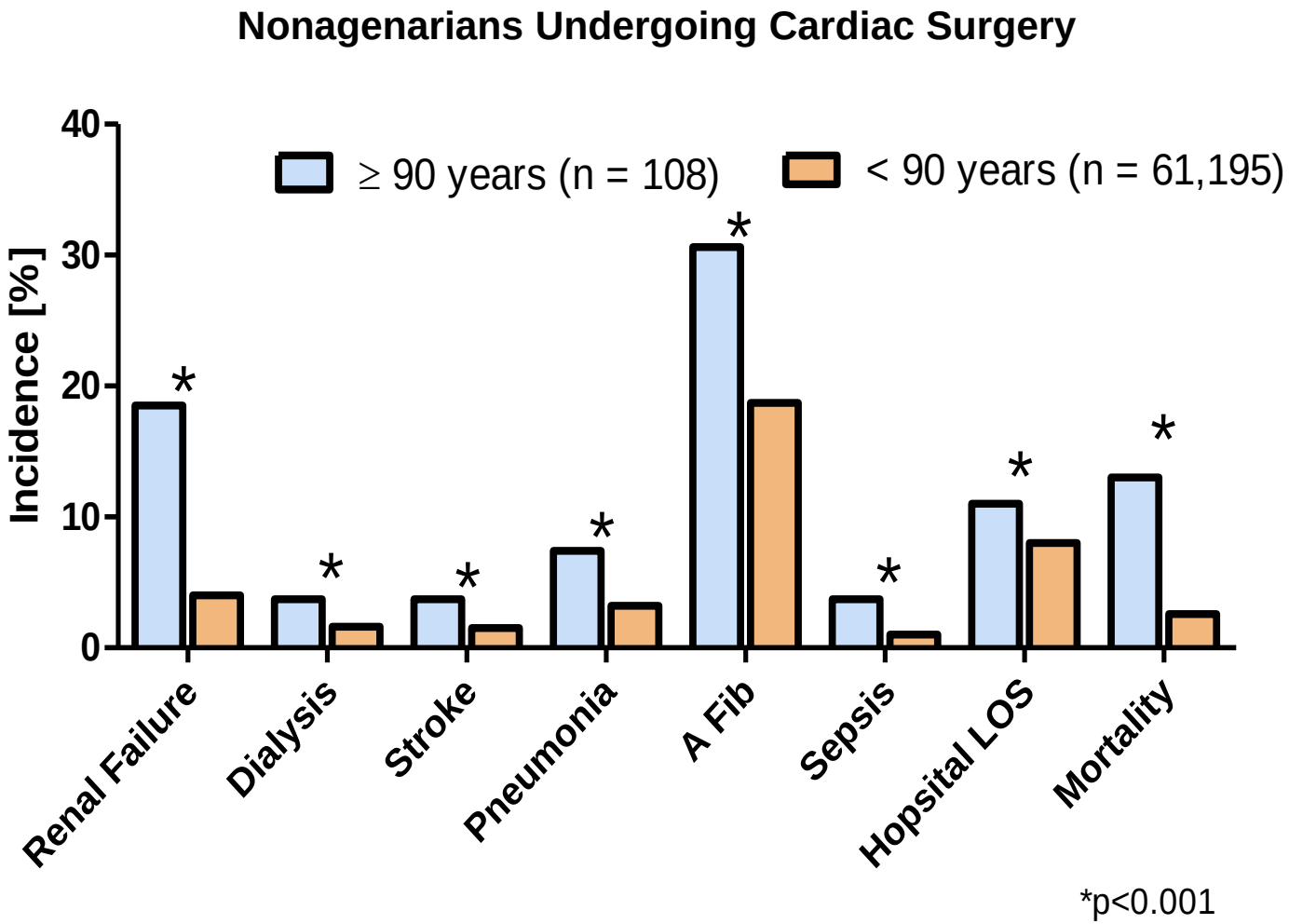


Myocardial Injury



N = 3,930 Ann Thorac Surg 2015

Outcome of the Elderly after CS



Davis et al , J Card Surg, 2014