Αορτοστεφανιαία παράκαμψη: με, χωρίς, λιγότερη εξωσωματική;

Γεώργιος Τσώνης, Καρδιοχειρουργός
Κλινική «Euromedica Κυανούς Σταυρός

Ιστορική αναδρομή

1916 Ionesco, διατομή αυχενικών συμπαθητικών νεύρων για ύφεση συμπτωμάτων στηθάγχης

1935 Beck & συν, προτείνουν αύξηση της αιμάτωσης με δημιουργία συμφύσεων μεταξύ επί- και περικαρδίου.

1946 Vineberg, εμφύτευση έσω μαστικής αρτηρίας εντός του μυοκαρδίου της ΑΚ

1957 Bailey & συν, Longmire & συν, ενδαρτηρεκτομή στεφανιαίων

1964 Favaloro & συν, Johnson & συν, αορτοστεφανιαία παράκαμψη

1968 Green – Kolessov, έσω θωρακική (μαστική) αρτηρία

1953 Gibbon CPB

Στα επόμενα χρόνια η αορτοστεφανιαία παράκαμψη με χρήση εξωσωματικής κυκλοφορίας εξελίχθηκε σε μια ασφαλή μέθοδο που προσέφερε άριστα αποτελέσματα και καλή ποιότητα ζωής σε εκατομμύρια ασθενείς.

Η CPB είναι γνωστό ότι συνοδεύεται από ένα σύμπλεγμα συστηματικών «φλεγμονωδών αντιδράσεων» που μπορεί να συνδυάζονται με λιγότερο ή περισσότερο σοβαρές μετεγχειρητικές επιπλοκές: νεφρικές , αναπνευστικές, νευρολογικές ή έχουσες σχέση με τον αιμοστατικό μηχανισμό.

Την προηγούμενη λοιπόν δεκαετία αναπτύχθηκε σταδιακά η τεχνική της αορτοστεφανιαίας παράκαμψης χωρίς τη χρήση εξωσωματικής κυκλοφορίας *(OPCAB) ή Beating Heart* προσδοκώντας να απαλλάξει τους ασθενείς από τις ανεπιθύμητες ενέργειες και τα συμβάματα που οφείλονται στην CPB.

Medtronic

Off Pump Coronary Artery Bypass Grafting

1995

OPCAB

Μετά την καθιέρωση της μεθόδου πολλές μελέτες έχουν γίνει προσπαθώντας να συγκρίνουν τις δύο τεχνικές σε σχέση με την θνητότητα , το έμφραγμα, τη βατότητα των μοσχευμάτων, την ανάγκη για επανεγχείρηση, τη νεφρική ανεπάρκεια αλλά και παραμέτρους που έχουν να κάνουν με το συνολικό κόστος όπως παραμονή στην κλινική, χρόνο αποδιασωλήνωσης και παραμονής στη ICU.

Επίσης έγινε προσπάθεια - ιδιαίτερα τα πρώτα χρόνια - να απαντηθούν ερωτήματα όπως :

Η εμπειρία του χειρουργού καθορίζει την επιλογή OPCAB ή CABG;

Πότε ο χειρουργός θα διακινδυνεύσει να θυσιάσει αριθμό ή βατότητα μοσχευμάτων για να «μάθει» μια καινούρια ενδεχομένως καλύτερη τεχνική;

Parolari et al meta analysis παρουσίασαν μια μεγάλη σειρά

CABG:558 ασθενείς
OPCAB:532 ασθενείς

έχοντας ως προς death, stroke, MI καλύτερα αποτελέσματα στην ομάδα OPCABG αλλά όχι στατιστικώς σημαντικά.

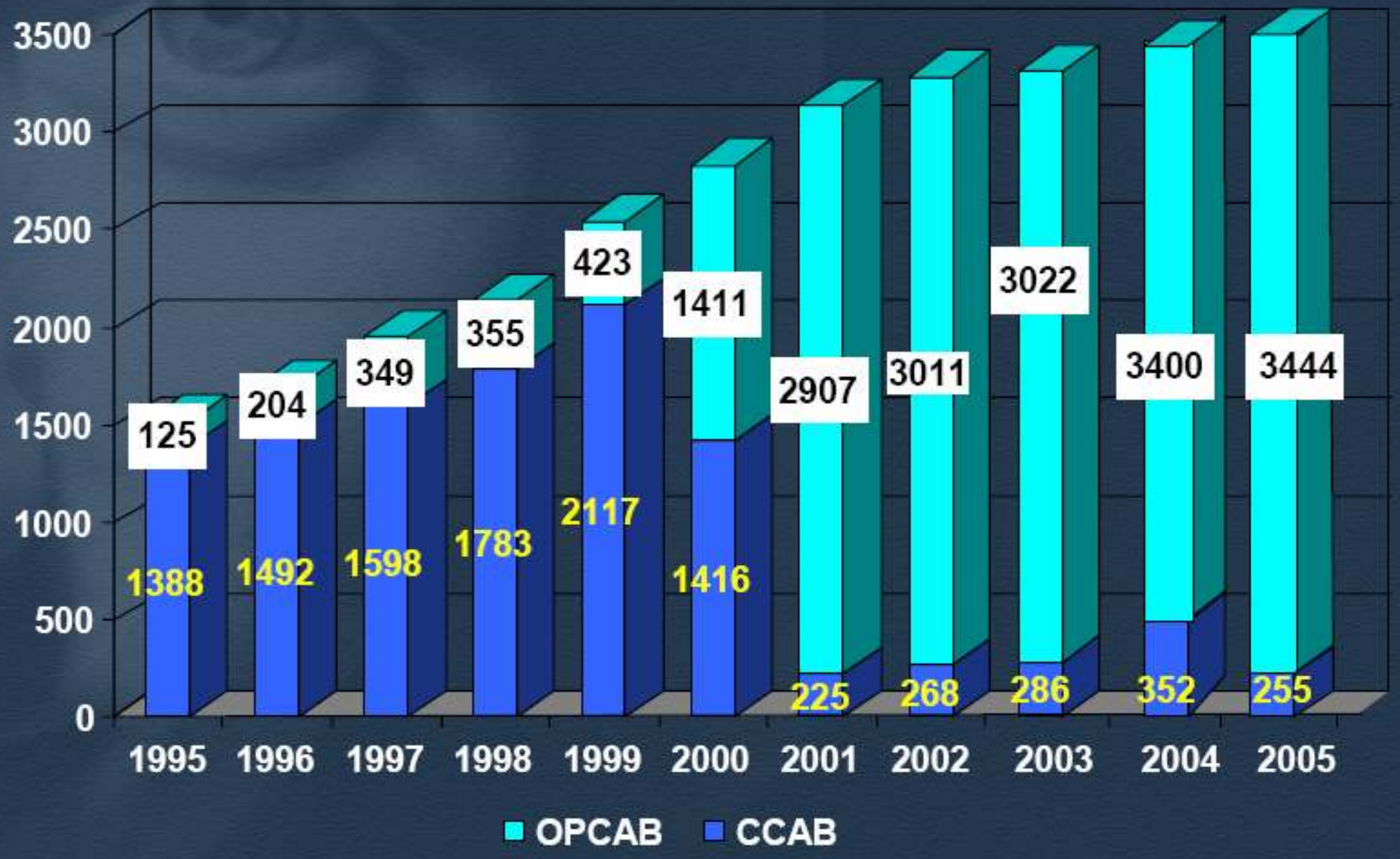
RCTs

Study details	Key efficacy findings	Key safety findings	Appraisal/Comments
Angelini *et al.* 2002[6], UK 200 off-pump (OPCAB); 201 onpump (CABG) March 1997 to November 1999 *Follow-up*: BHACAS 1: 25 [9.1] months; BHACAS 2: 13.7 [5.5] months *Selection criteria*: Exclusions: LVEF <30; history of supraventricular arrhythmia; previous CABG; renal or respiratory impairment; previous stroke, transient ischaemic attack or coagulopathy. BHACAS 1 also excluded patients with recent MI or who required grafting of the circumflex artery distal to the first obtuse marginal branch	Pooled survival estimate at 24 months: OPCAB 97% (95% CI 92 to 99) CABG 96% (95% CI 91 to 98) Hospital stay > 7 days: RR 0.54 (95% CI 0.36 to 0.80) in favour of OPCAB	Hazard ratio for all cause mortality 0.57 (95% CI 0.17 to 1.96) Myocardial infarction: RR 0.20 (95% CI 0.02 to 1.69) Atrial fibrillation: RR 0.34 (95% CI 0.23 to 0.51) in favour of OPCAB Chest infection: RR 0.39 (95% CI 0.22 to 0.68) in favour of OPCAB Blood loss >1000 ml: RR 0.66 (95% CI 0.47 to 0.94) in favour of OPCAB	*Potential for bias*: allocation concealment was adequate (numbered, sealed, opaque envelopes); patients blinded to treatment allocation; outcome assessors blinded for some outcomes; intention-to-treat analysis done; *a priori* power and size calculations done; 6 patients were lost to follow-up (data censored at time of last contact) and 11 patients died (censored at time of death) *Outcome measures and their validity*: majority of outcome measures were objective *Other comments*: this article pools 2 RCTs – BHACAS 1 and 2 (Beating Heart Against Cardioplegic Arrest Study); exact type of stabilisers used not clear, therefore results may not be comparable to the MSAC review which only included mechanical stabilisers
Caputo *et al.* 2002[7], UK 60 patients – 20 CPB on-pump, 20 off-pump, 20 off-pump with right ventricular assistance (RVAD) *Follow-up*: not stated but only perioperative outcomes given *Selection criteria*: Included: First-time CABG; Excluded: cardiac ejection fraction <0.30, recent MI, type II diabetes, coagulopathy and previous CVA, respiratory or renal failure	Operative time was significantly longer in the on-pump groups (230 minutes 95% CI 209 to 250) compared with the off-pump (184 minutes 95% CI 158 to 211, p=0.007) and off-pump with RVAD (192 minutes 95% CI 178 to 205), p=0.003). No statistically significant differences in ventilation time, ICU and hospital stay were detected between the three groups. Central venous pressure increased significantly only in the off-pump group. On-pump patients showed a greater inflammatory response (as measured by a number of biochemical markers) and while no difference could be detected between the off-pump and the off-pump with RVAD groups, these patients did show some inflammatory response.	No hospital deaths or major postoperative complications occurred in any of the three groups. No statistically significant differences in incidence of arrhythmias, wound infections, neurologic and respiratory complications, and blood loss were detected between the three groups.	*Potential for bias*: adequate allocation concealment (sequentially numbered, sealed, opaque envelopes); blinding of patients and outcomes assessors not stated; losses to follow-up not stated; however it was stated that some missing data were imputed; *a priori* power calculations were done. *Outcome measures and their validity*: Haemodynamic stability not reported (only central venous pressure) limiting the interpretation of the role of RVAD in reducing haemodynamic instability *Other comments*: not stated if stabiliser is pressure or suction "reusable stainless steel stabiliser"

Study details	Key efficacy findings	Key safety findings	Appraisal/Comments
Puskas 2002[10], USA Dates: not stated 200 patients (100 off-pump; 100 on-pump) – SMART (Surgical Management of Arterial Revascularization Therapies) study *Follow-up*: not stated *Selection criteria*: not stated	Number of grafts: "virtually identical" for off-pump and on-pump and equally effective in restoring blood flow Hospital stay: one less day for off-pump compared to on-pump Ventilator time: less for off-pump than on-pump	Death, MI or stroke: similar or lower rates with off-pump compared to on-pump Blood loss and need for transfusions: less for off-pump than for on-pump Damage to heart muscle during surgery: less for off-pump than on-pump	*Potential for bias:* Not possible to assess as data were taken from 2 media releases. However these stated that as many participants as possible were blinded and that the same surgeon treated all patients. *Outcome measures and their validity*: all off-pump patients received all grafts necessary to achieve complete revascularisation *Other comments*: Quantitative results not presented in media releases; Octopus suction stabiliser used for off-pump procedure
van Dijk *et al.* 2001/2002[8,9], NETHERLANDS March 1998 to August 2000 281 patients (265 treated according to randomisation) - 142 off-pump; 139 on-pump *Follow-up*: 12 months *Selection criteria*: Included: first-time isolated CPB, off-pump deemed technically feasible=predominantly 1 or 2 vessel disease Excluded: emergency or concomitant major surgery, recent MI, poor LVF or unlikely to complete 1 year follow-up	Completeness of revascularisation: no differences detected between off-pump and on-pump Cognitive decline (12 months) n=248: RR 0.88 95% CI 0.52 to 1.49; 30.8% off-pump 33.6% on-pump Quality of life: No statistically significant differences between off-pump and on-pump at 12 months; both groups reported a marked improvement at 3 months, with only bodily pain and general health perceptions showing further improvement at 12 months	Mortality (all cause): no statistically significant difference at 12 months (2 per group) Stroke rate: no statistically significant difference at 12 months	*Potential for bias*: adequate allocation concealment (telephone randomisation) and this was also tested with logistic regression; outcome assessors blinded, but not surgeons or patients; intention-to-treat analysis (10 patients allocated to off-pump underwent on-pump; 1 off-pump patient underwent angioplasty; 5 patients allocated to on-pump underwent off-pump); 29/281 (10.3%) were lost to follow-up at 12 months – 12 off-pump, 17 on-pump; *a priori* power calculations were done; sensitivity analyses and imputation carried out for missing data; patients were more likely to be low-risk than the general population undergoing OPCAB, and this is a potential threat to external validity *Outcome measures and their validity*: Cognitive outcome was measured by a battery of 10 neuropsychologic tests (in accordance with the Statement of Consensus on Assessment of Neurobehavioral Outcomes after Cardiac Surgery); Quality of Life was measured by EuroQol and SF-36, both validated *Other comments*: In 8% of off-pump patients access was via left anterior thoracotomy instead of sternotomy

Κάποιες ανακοινώσεις που προσπάθησαν να μελετήσουν τις επιπτώσεις στο αναπνευστικό σύστημα, έδειξαν *καλύτερα αποτελέσματα στην OPCAB* ως προς τα αέρια αίματος και τον χρόνο αποδιασωλήνωσης, αλλά και *καμιά διαφορά* στην α/α θωρακα, σπιρομέτρηση, συχνότητα θανάτων, πνευμονίας, πλευριτικών συλλογών ή πνευμονικού οιδήματος.

Growth of OPCABs : 1995 - 2005



PROCAB FOLLOW UP
Grafts Evaluation: FitzGibbon Score

Variable	Total No. of grafts	OPCAB n=62	CCAB n=52	P value
No. of Grafts	338	186	152	-
FitzGibbon A	317(93.78%)	174	143	0.980
FitzGibbon B	6(1.77%)	4	2	0.870
FitzGibbon O	15 (4.45%)	8	7	0.980

FitzGibbon A – Perfectly Patent
FitzGibbon B – Any stenosis of less than 50% of the diameter of the target coronary artery
FitzGibbon O – Totally Occluded

PROCAB
Study Conclusions

- Good outcome with either of the procedure.
- Mean no of grafts was similar in both groups.
- Rates of mortality, perioperative MI, stroke, renal failure & angina were similar.
- No difference in the rate of reinterventions.
- Graft patency at one year was similar in both group
- In OPCAB there was:

  Reduced blood loss & transfusion requirement ,

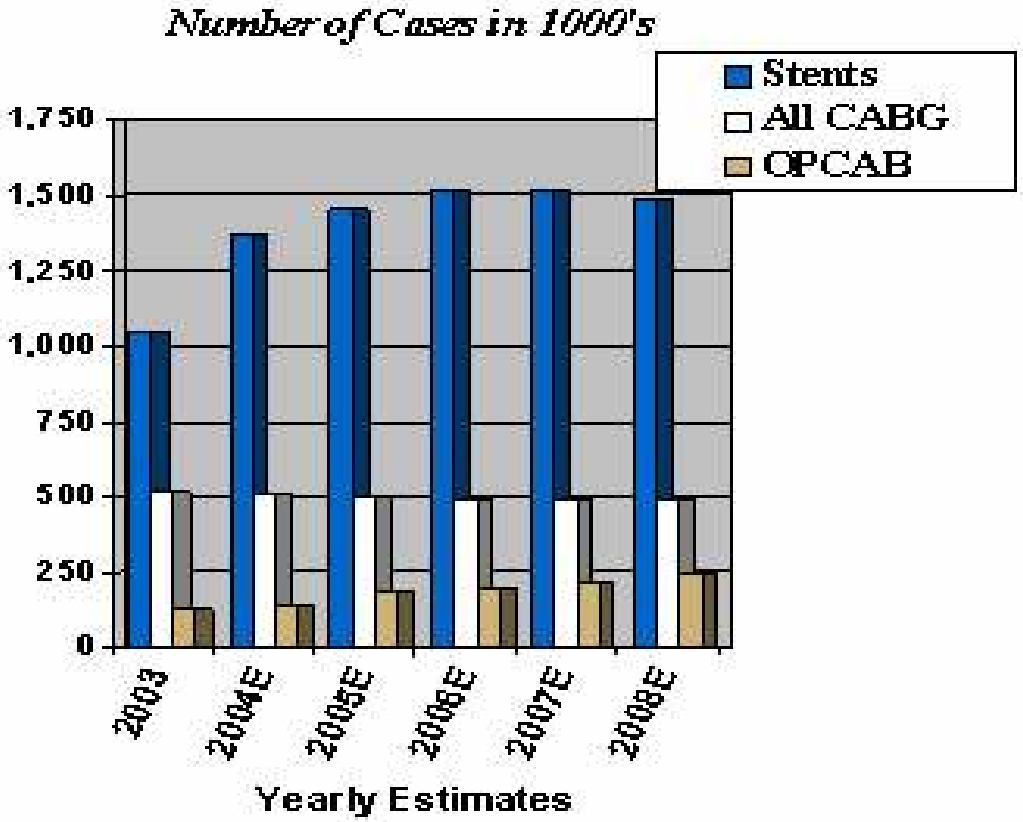
  Reduced duration of ventilation & shorter hospital stay.

  Reduced Myocardial enzymes release

  Reduced incidence of neurological events

OPCAB…A New Standard of Care

WW Revascularization Market



Total CABG procedures are declining (2, 7)

Beating Heart CABG procedures have increased, and are expected to represent 50% of CABG by 2008 (2)

The use of drug eluting stents is expected to level off starting in 2005 with the emergence of new technologies (1,3,6)

MORE EVIDENCE

OPCAB- A New Standard of Care

CPB has been shown to produce adverse effects in patients undergoing myocardial revascularization – particularly in high-risk patient groups.

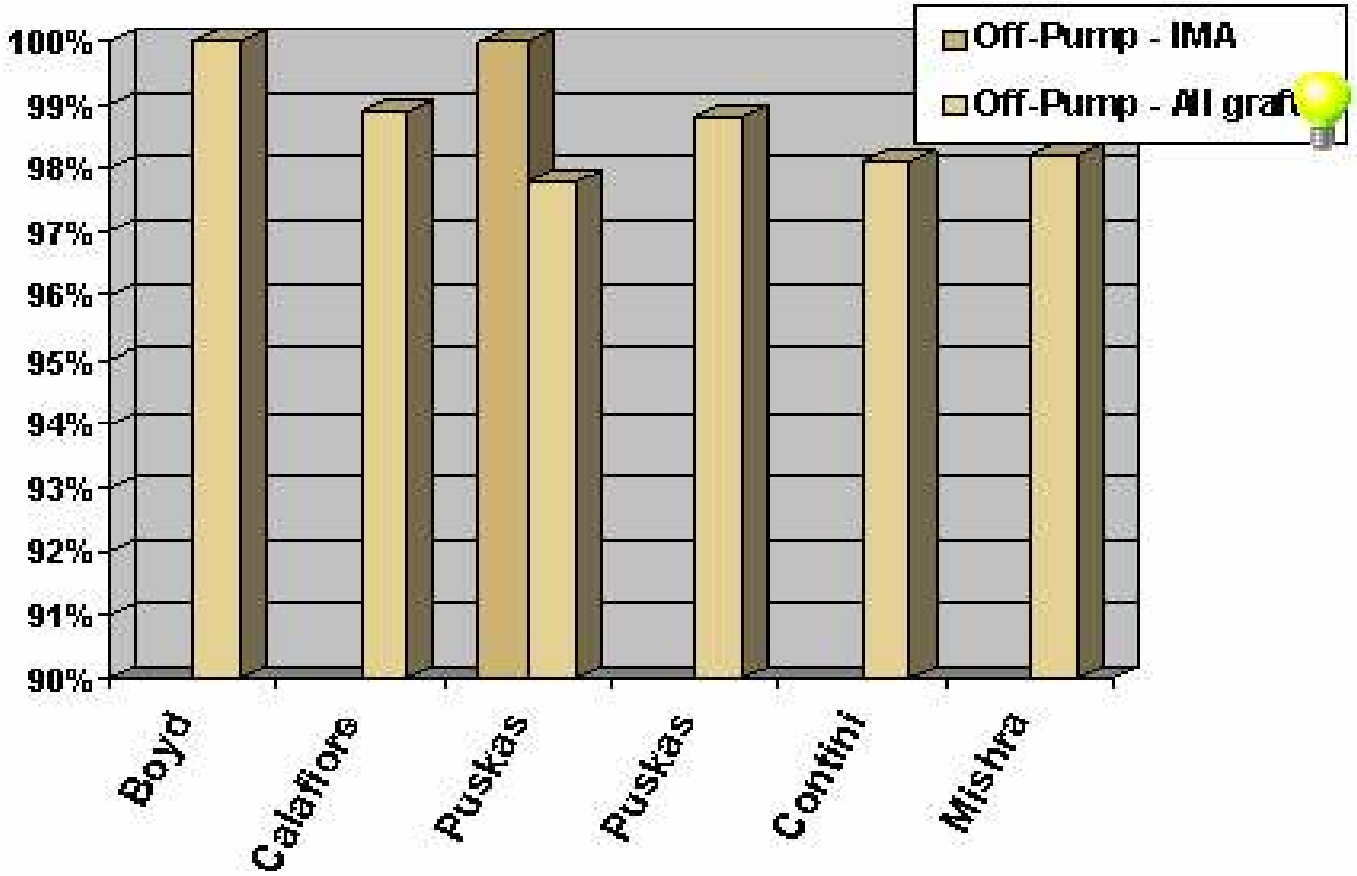
OPCAB studies over the last several years, from around the world, have demonstrated equal patency with fewer morbid events when compared to conventional CABG (cCABG). (Haase STS 2003)

- Complete revascularization (# of grafts) has been demonstrated for both on- and off-pump patients. (Puskas J, Presented at AATS 2002; Hart James C, STS 2003)
- Demonstrated benefits from the growing body of evidence supporting OPCAB includes:

Reduced use of blood products	Less postoperative stroke
Less myocardial damage	Less instance of Atrial Fibrillation
Reduced morbidity and mortality	Less chest drainage
Shorter length of stay	Fewer neurocognitive disorders

Several studies have also indicated OPCAB costs less than traditional CPB.

Equivalent Patency



Patency rates in off-pump CABG procedures have been shown in several clinical series to be equal to or greater than those of cCABG

See Attached Bibliography for supporting references

BHACAS – graft patency

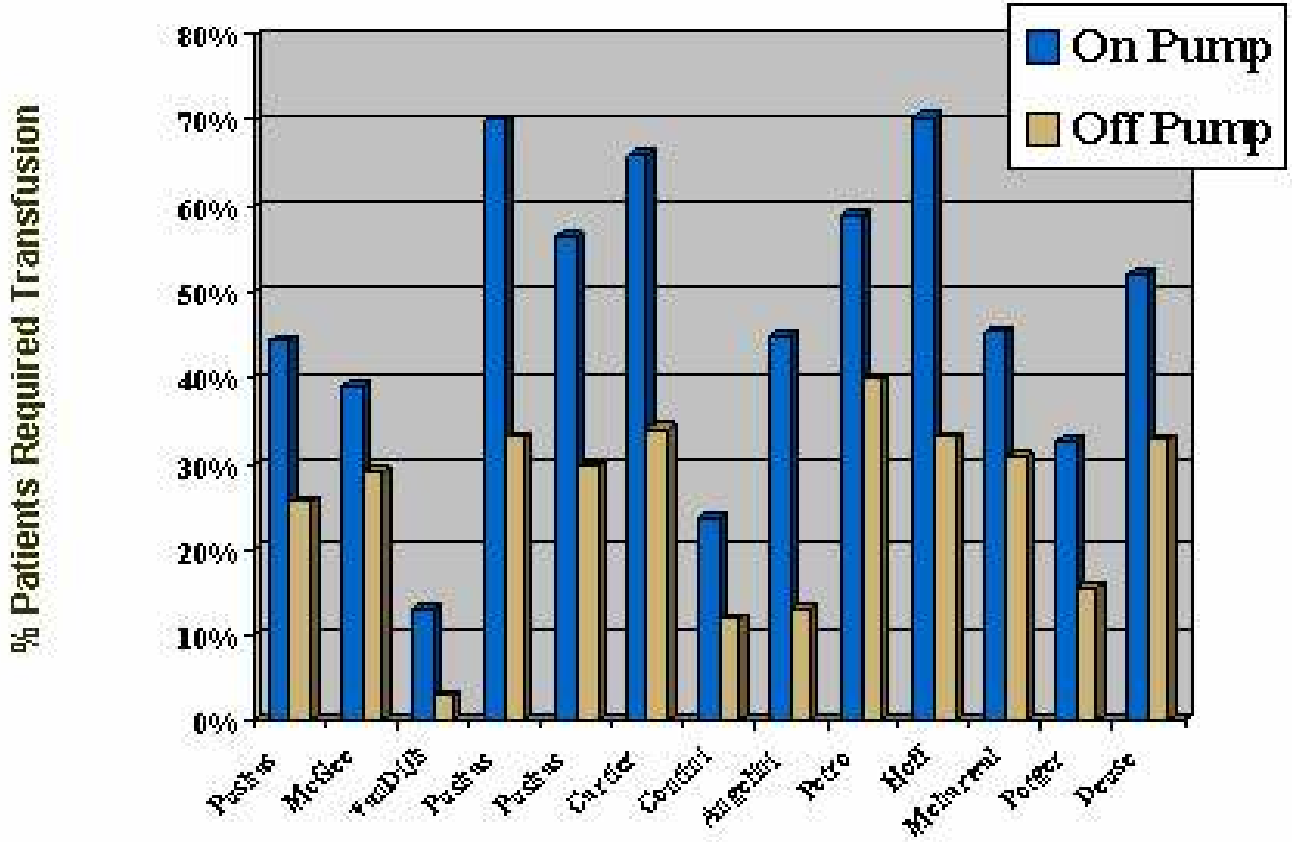
CABG-CPB (n=101)		OPCAB (n=98	
Total no. of grafts	Patent	Total no. of grafts	Paten
263	224 (85.2 %)	238	204 (85.7

Graft Patency Rates

OPCAB vs conventional CABG

Graft	Time	OPCAB (n = 240)	Conv- CABG (n = 109)	P-VALUE
ITA	1-Y	504/527(95.6)	141/144(97.9)	0.328
	5-Y	487/527(92.4)	130/144(90.3)	0.489
SVG	1-Y	92/121(76.0)	187/227(82.4)	0.161
	5-Y	90/121(74.4)	182/227(80.2)	0.222

Reduced Transfusion Rates



Studies have demonstrated less blood loss and reduced need for transfusion when bypass surgery is done off-pump.

Reduced transfusion requirements can lead to:

- **Reduced (transfusion) complications**
- **Reduced risk of disease transmission (HIV and hepatitis)**
- **Lower health care costs ($300 - $1,000 / unit of blood)**
- **Less burden on the limited national blood supply**

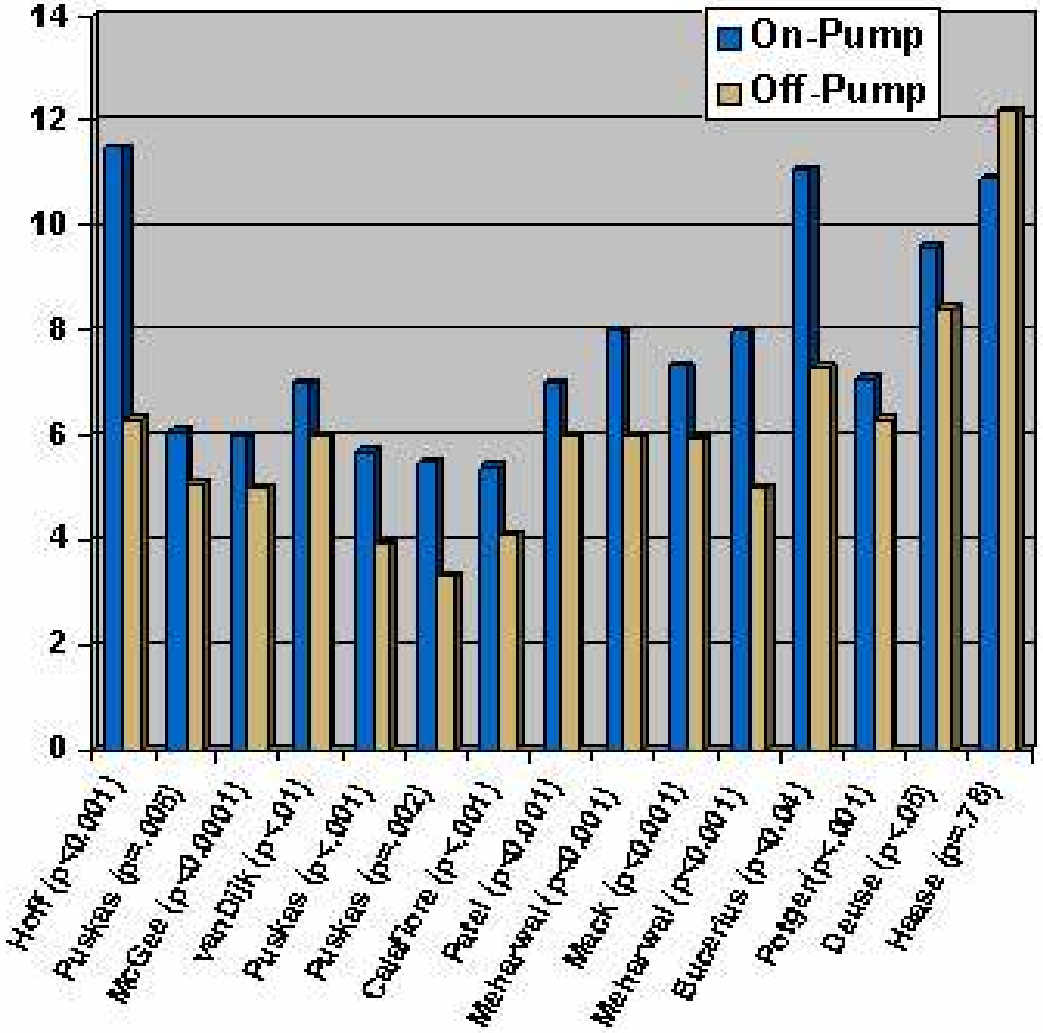
See Attached Bibliography for supporting references

Prospective, Randomized Trials of OPCAB vs Conventional On-Pump CABG; *Transfusions*

Trials	OPCAB		On-Pump CABG	
	#	Transfusion (%)	#	Transfusion (%)
Van Dijk (NEJM 2003)	142	28	139	29
Angelini (Lancet 2002)	200	18	201	49
Puskas (JTCVS 2003)	98	26	99	44
PRAGUE-4 (ATS 2004)	204	49	184	51
Khan (NEJM 2004)	54	37	50	65
TOTAL	698	31%	698	45%

$p < 0.01$

Shortened Length of Stay



- Trend toward earlier extubation of patients
- Shorter ICU stays
- Faster patient recovery
- Reduced length of stay contributes significantly to overall reduction in hospital costs

See Attached Bibliography for supporting references

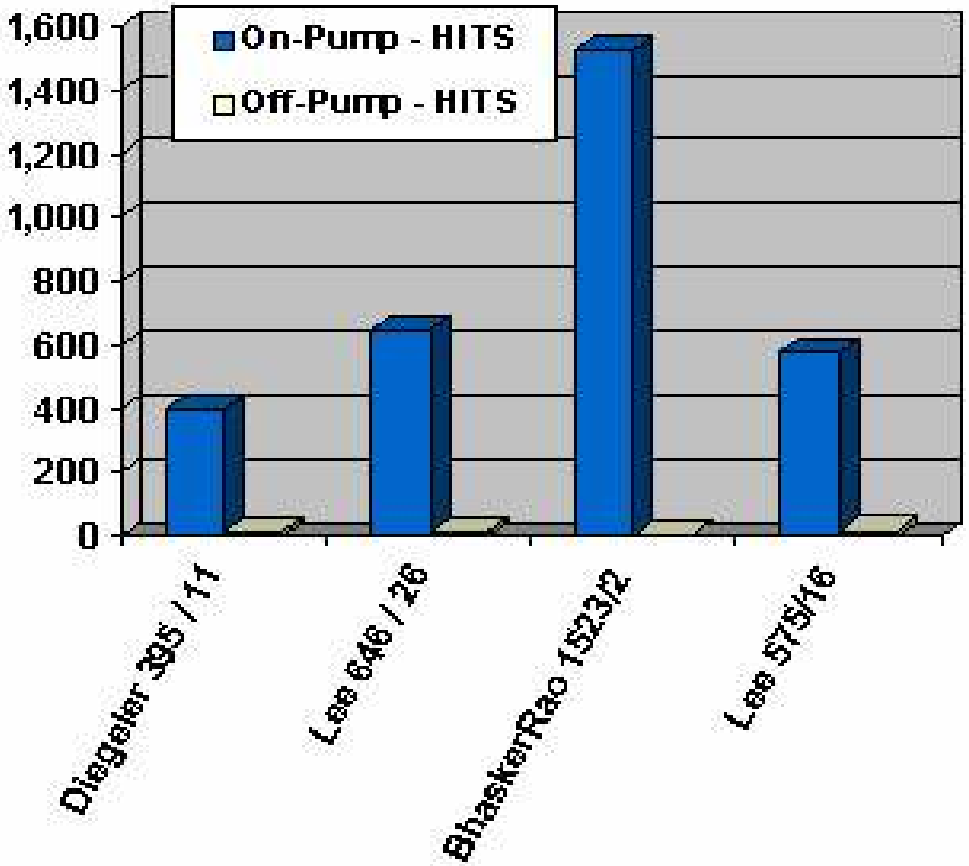
Prospective, Randomized Trials of OPCAB vs Conventional On-Pump CABG; *Atrial Fibrillation*

Trials	OPCAB		On-Pump CABG	
	#	AF (%)	#	AF (%)
Van Dijk (NEJM 2003)	-	-	-	-
Angelini (Lancet 2002)	200	12	201	37
Puskas (JTCVS 2003)	98	16	99	22
PRAGUE-4 (ATS 2004)	204	20	184	24
Khan (NEJM 2004)	-	-	-	-
TOTAL	502	15%	484	29%

$p < 0.01$

Reduced Cognitive Impairment

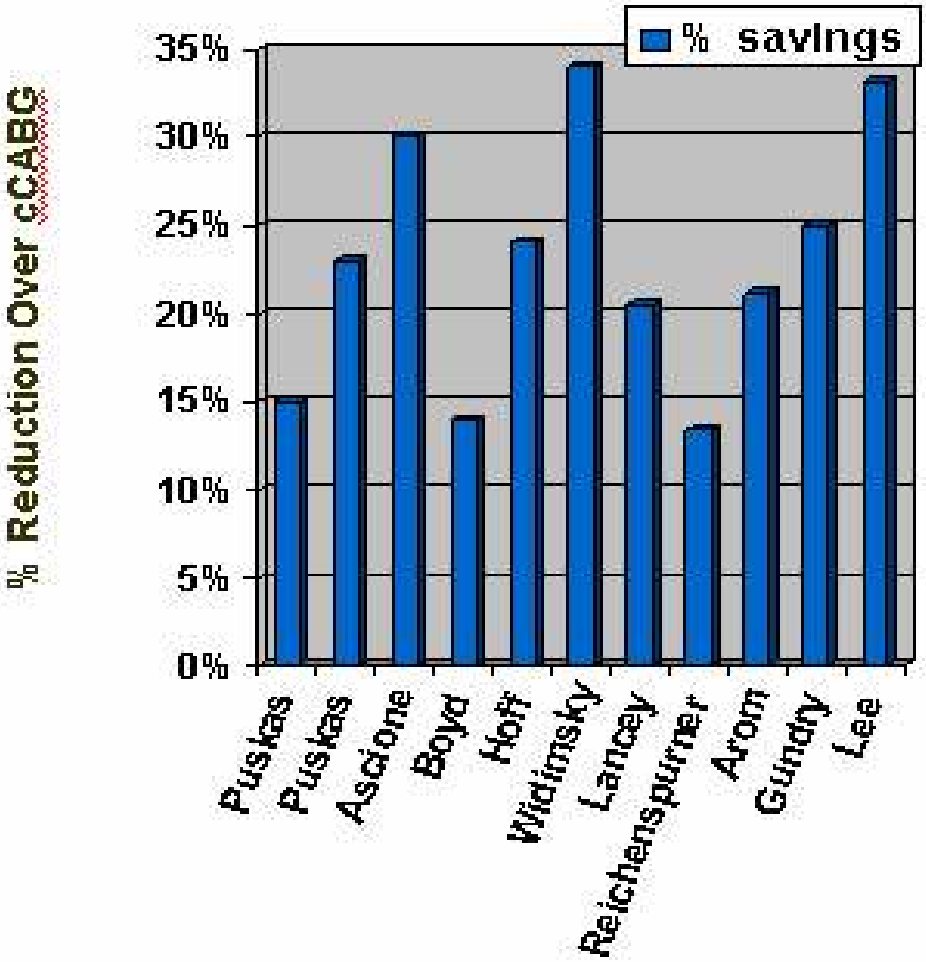
HITS - Micro-emboli Measured in the Brain



Off-pump patients incurred a significantly reduced number of HITS (High Intensity Transcranial Doppler Signals) vs. on-pump population

See Attached Bibliography for supporting references

Reduced Hospital Costs

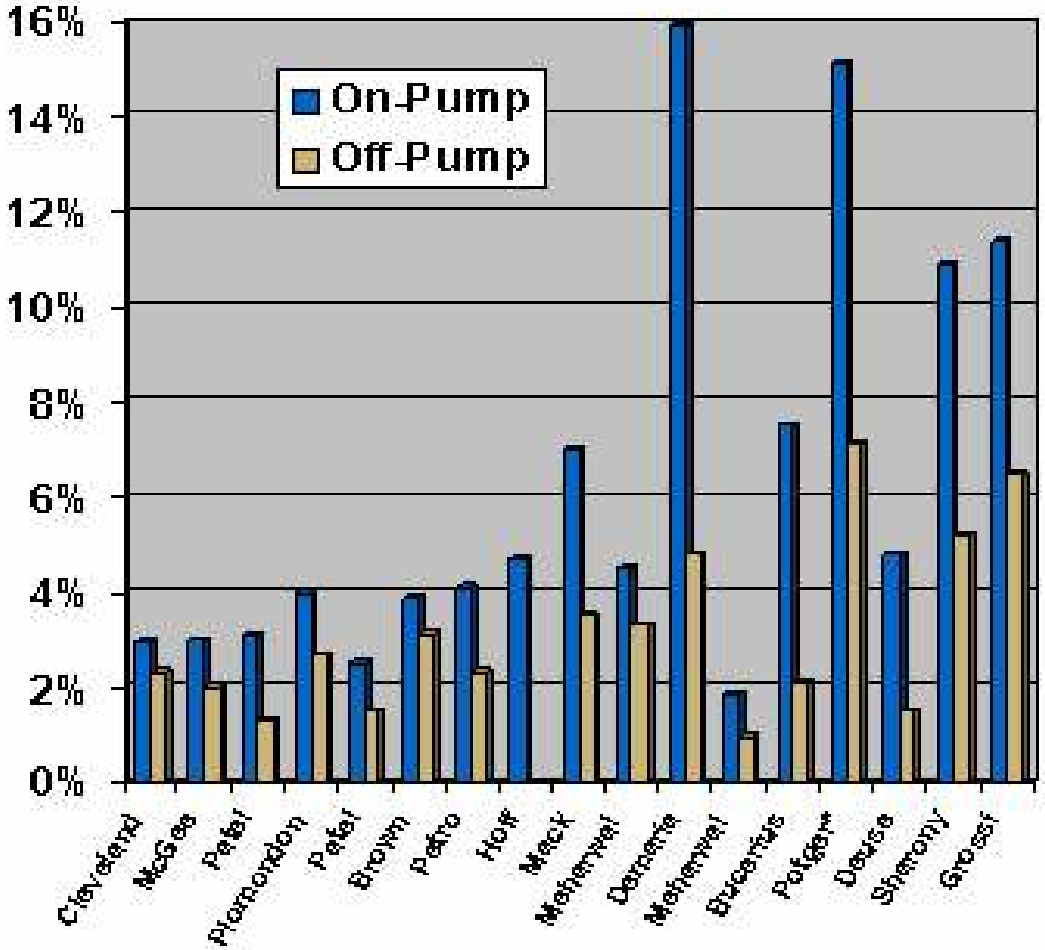


OPCAB has been shown to help hospital systems realize significant cost reductions due to:

- Less time in the ICU
- Shorter Hospital Stay
- Shorter Surgery Times
- Fewer blood transfusions
- Reduced morbidity and mortality

See Attached Bibliography for supporting references

Reduced Mortality



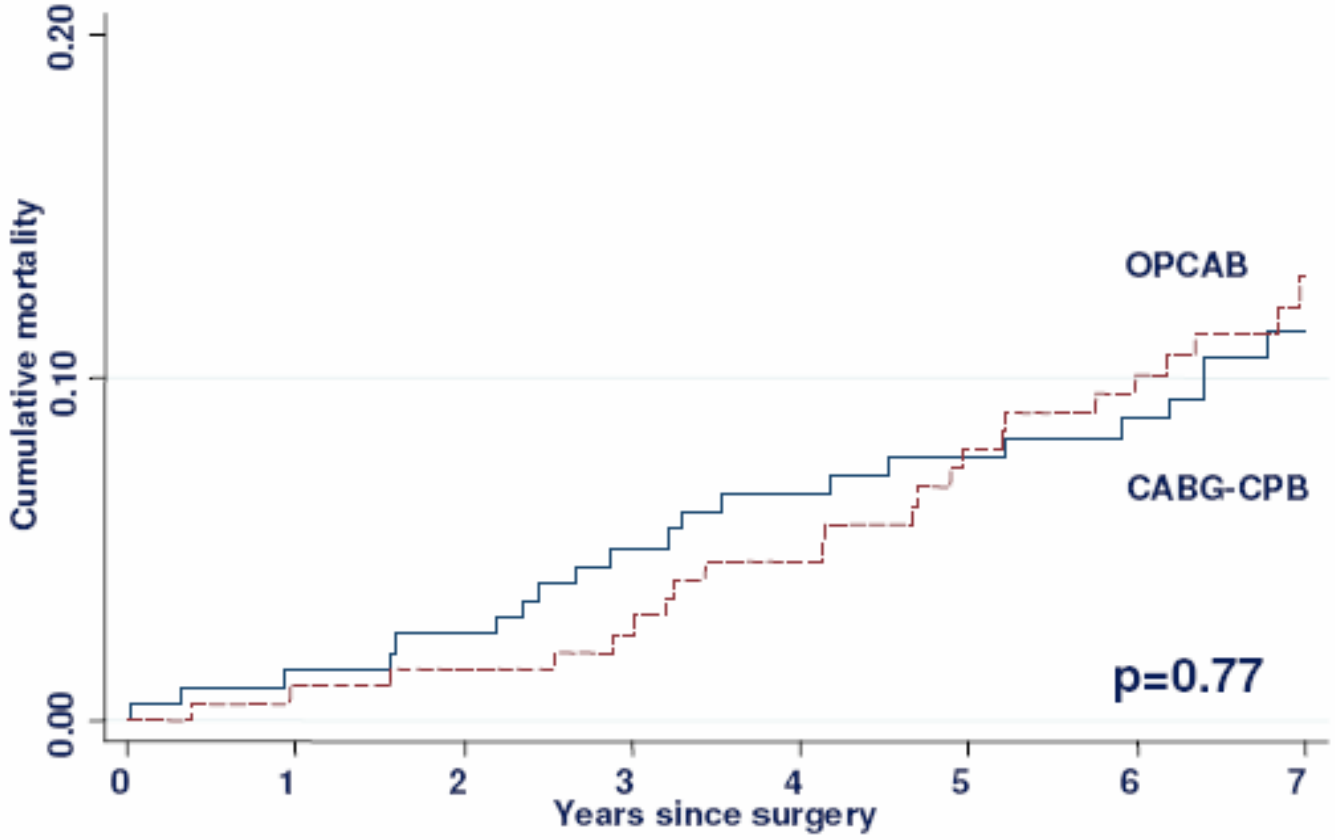
Several large retrospective studies have demonstrated a significant reduction in mortality for OPCAB patients

Off-pump CABG carries a significantly lower mortality rate in the high-risk population vs. cCABG (Arom 2000)

*High Risk patients

See Attached Bibliography for supporting references

Patient survival

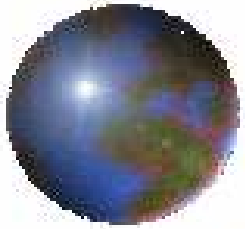


Number at risk								
CABG-CPB	201	198	195	185	178	166	158	93
OPCAB	200	197	195	187	178	171	160	93

Prospective, Randomized Trials of OPCAB vs Conventional On-Pump CABG; *Mortality*

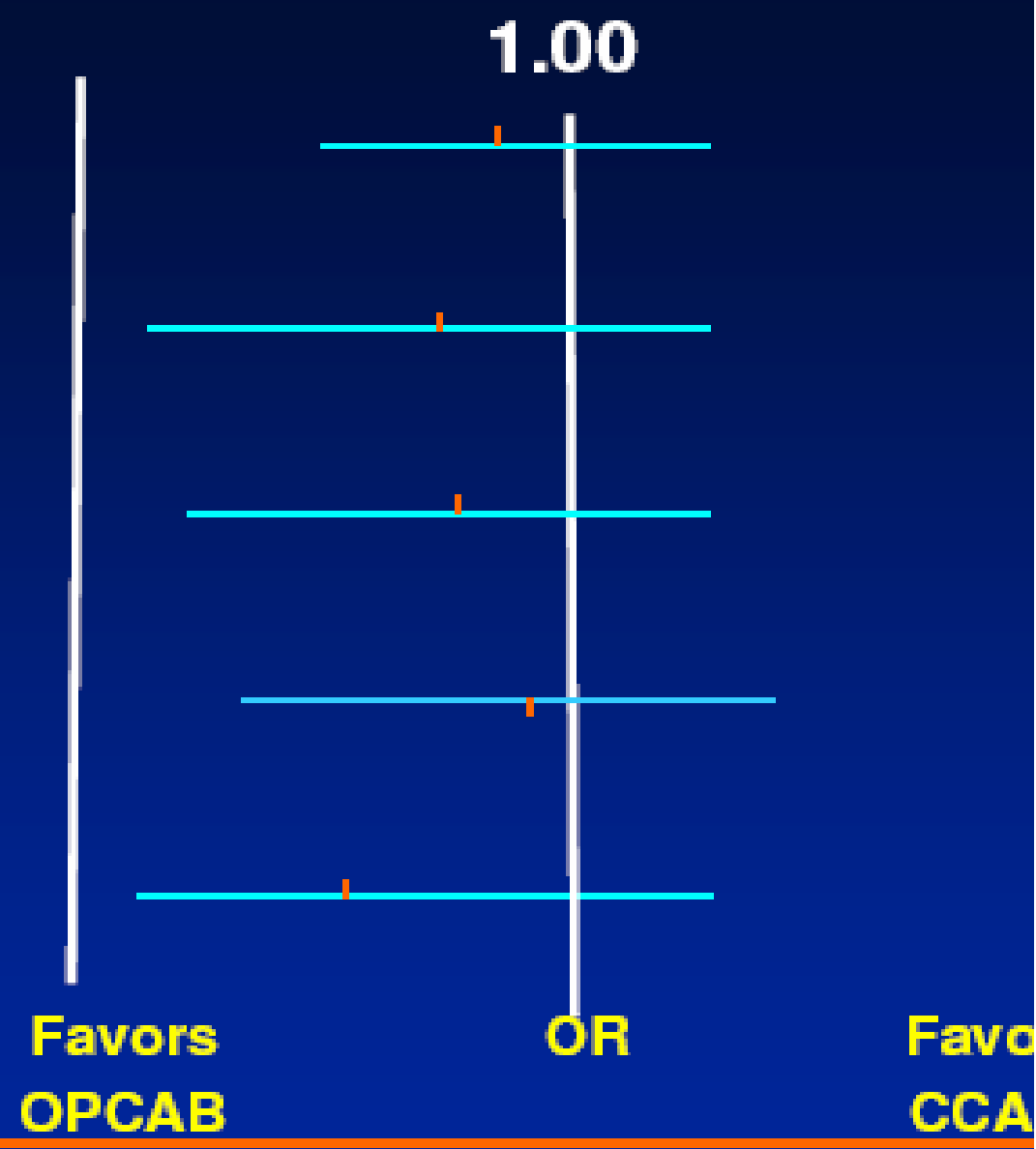
Trials	OPCAB		On-Pump CABG	
	#	Mortality	#	Mortality
Van Dijk (NEJM 2003)	139	0	142	0
Angelini (Lancet 2002)	201	2	200	0
Puskas (JTCVS 2003)	99	2	98	1
PRAGUE-4 (ATS 2004)	184	2	204	4
Khan (NEJM 2004)	50	0	54	0
TOTAL	673	6 (0.9%)	698	5 (0.7%)

OPCAB…



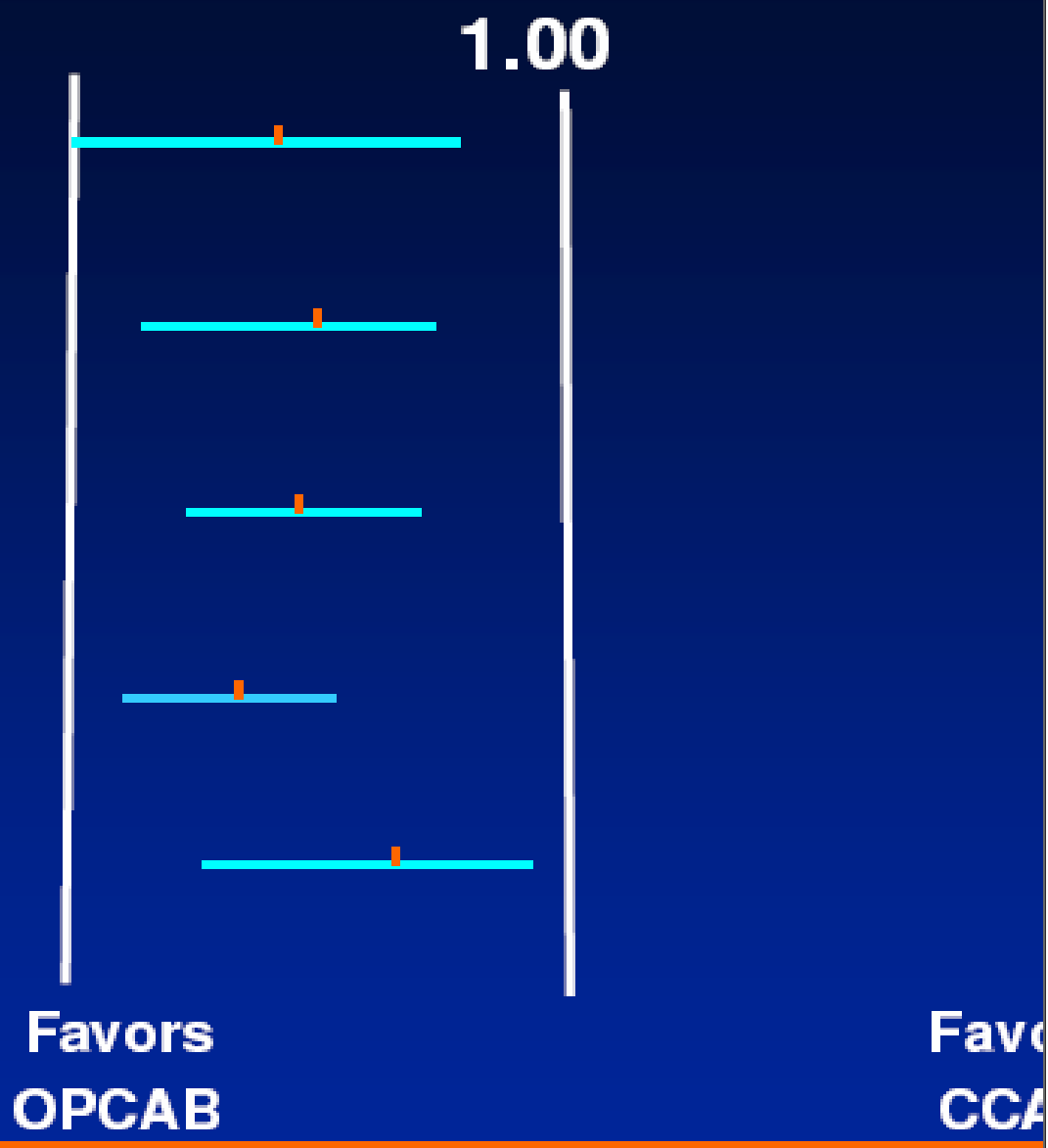
The New Standard of Care!

Death	29 RCTs
Stroke	21 RCTs
AMI	24 RCTs
Reop	15 RCTs
Renal Failure	10 RCTs



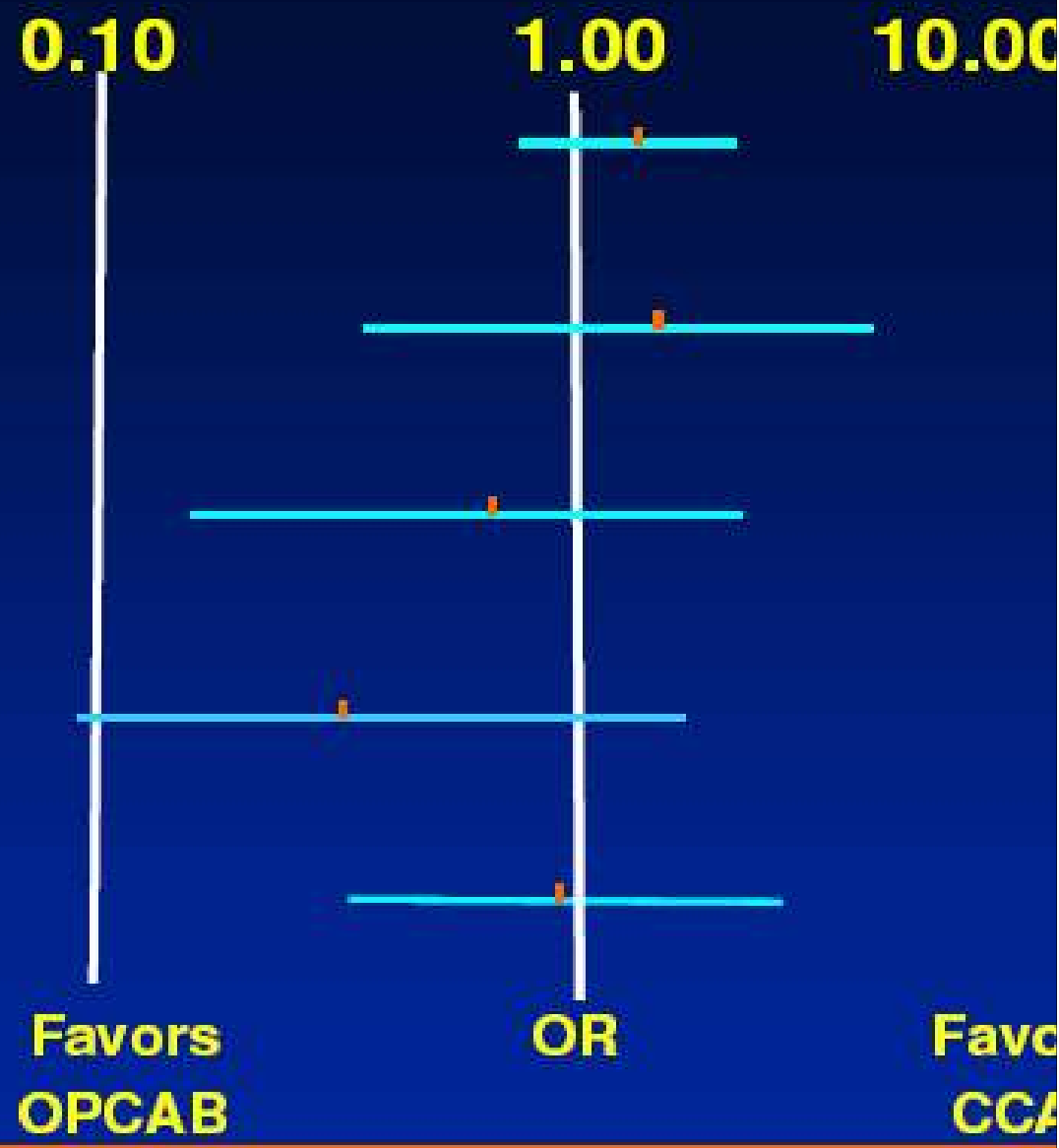
OPCAB v CCAB: Clinical Outcomes at 30 days – Level A

Transfusion	16 RCTs
AF	16 RCTs
Inotropes	14 RCTs
Resp Infxn	6 RCTs
LOS	12 RCTs

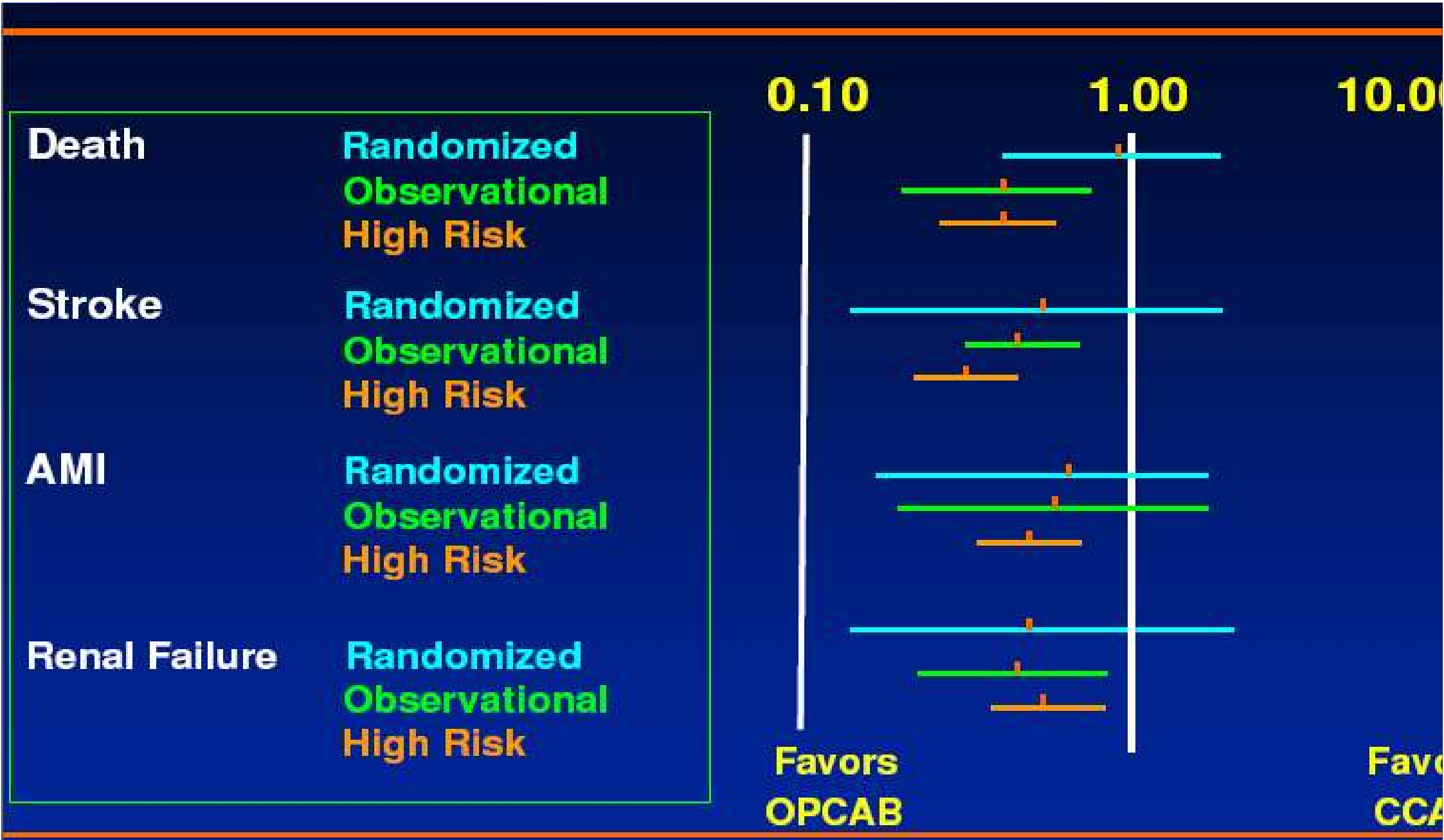


OPCAB v CCAB: Clinical Outcomes at 30 days – Level A

Angina Recur 1-2yrs	2 RCTs
Re-intervention 1-2yrs	6 RCTs
Mortality 1-2yrs	6 RCTs
Stroke 1-2 yrs	4 RCTs
Neurocognitive Dysfunction 1-2yrs	2 RCTs



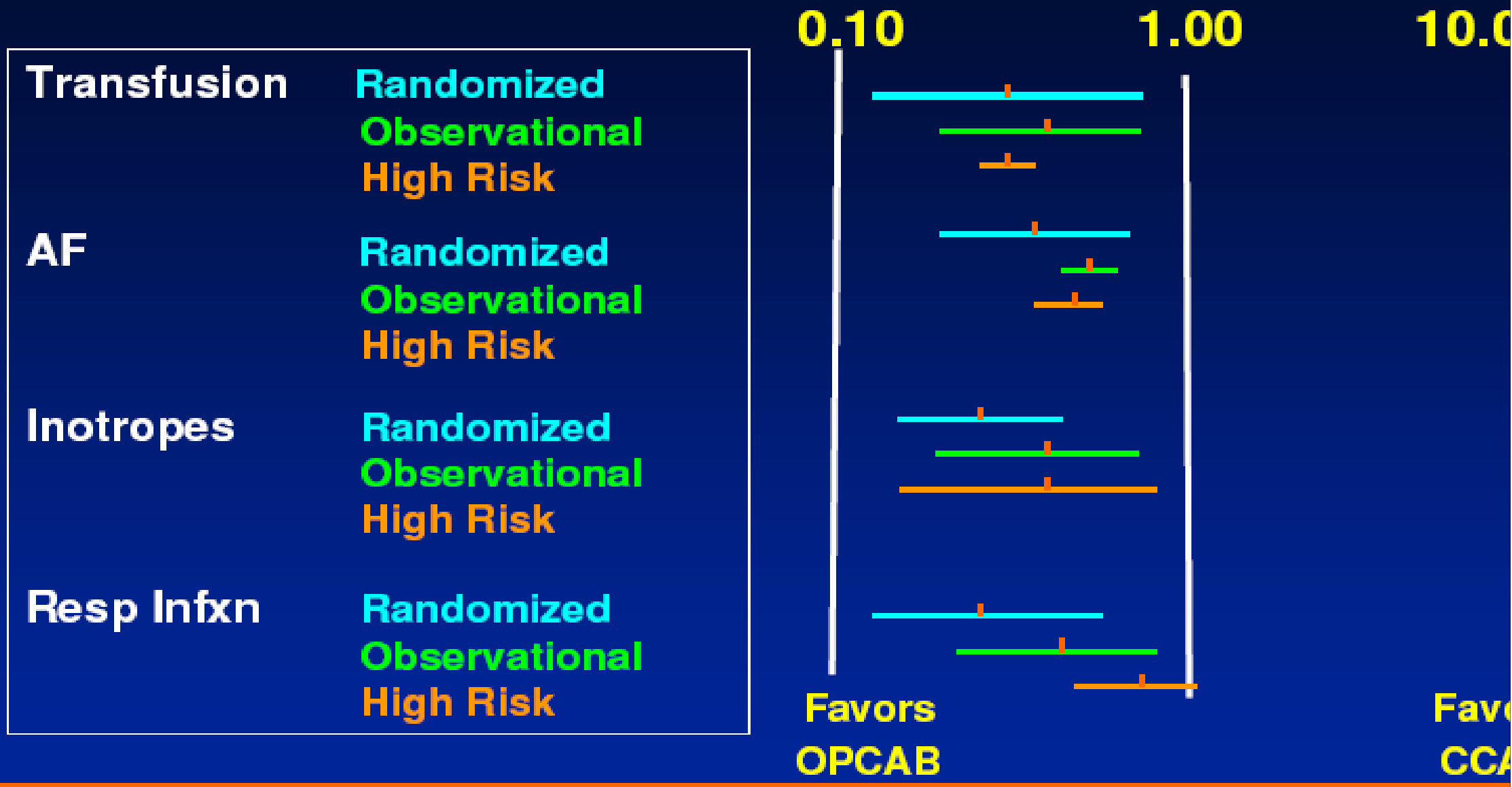
OPCAB v CCAB: Clinical Outcomes at 1-2 years – Level A



OPCAB v CCAB: RCT, NRCT, High-Risk Pt Studies

Cheng 2005 (35 RCTs; 3305 pts) - Beattie 2004 (16 NRCTs; >250k) or

Reston 2003 (53 trials; >39k) ISMICS Consensus 2004 (45 NRCTs; >26k)



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Reston 2003 (53 trials; >39k) - ISMICS Consensus 2004 (45 NRCTs; >26k)

Training !

THEY SAY YOU CAN'T TEACH AN OLD DOG NEW TRICKS...
BILL C.

Μετατροπή OPCAB →on pump

Αιμοδυναμική αστάθεια **Μικρά αγγεία** **Θέση αγγείων**	**35% LAD, Diag** **40% Cx** **10% RCA**	**↑ Θνητότητα, νοσηρότητα** **↑ Ινότροπη υποστήριξη** **↑ Μετάγγιση αίματος**

Third Generation of Cardiac Surgery

ROBOTICS

2002

ADVANTAGES OF ROBOTICS

- No Sternotomy
- No CPB
- Enhances Surgical Dexterity
- Computer Elimination of Tremors
- Motion Scaling

LAD+Diagonal TECAB

ΣΥΖΗΤΗΣΗ - ΣΥΜΠΕΡΑΣΜΑΤΑ

- Ασφαλής
- Συντριπτικά βιβλιογραφικά δεδομένα
- Εύκολη; - training
- Εναλλακτικά : Beating heart – on pump