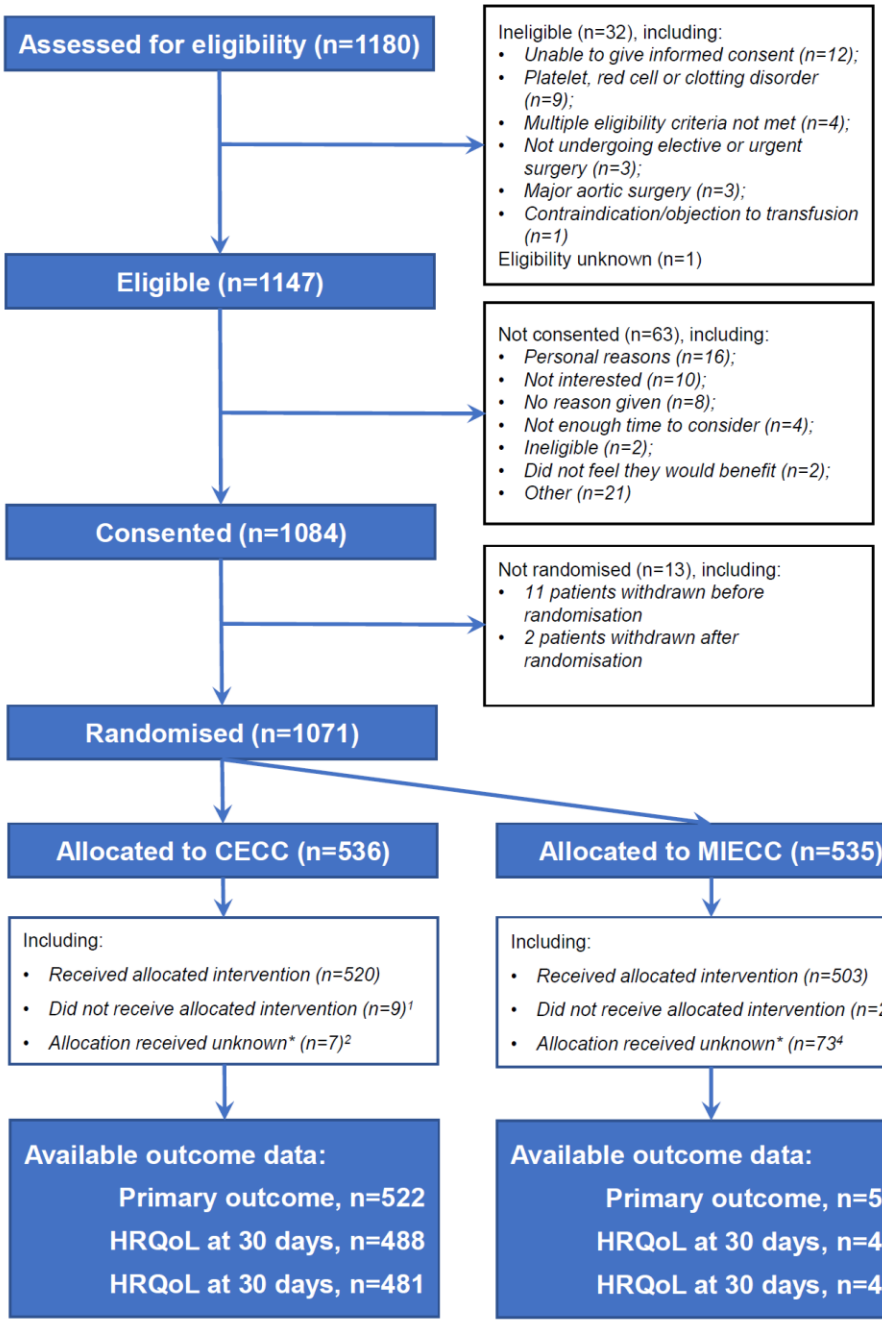
Conventional versus Minimally Invasive extra-corporeal circulation in patients undergoing Cardiac Surgery: a randomized controlled trial (COMICS)

ISRCTN 92590475



[1] 2 [1] 2 patients received MiECC and 7 patients did not received either MiECC or CECC (5 withdrew before the operation).

[2] 6 patients who withdrew before the operation.

[3] 18 patients received CECC and 11 patients did not received either MiECC or CECC (5 withdrew before the operation).

[4] 5 patients who withdrew before the operation.

Figure 1: flow of patients in the trial

Table 1 Patient demography, medical history, pre-operative medications and operations

	Randomised to CECC (n=536)		Randomised to MiECC (n=535)		Overall (n=1071)	
	n	%	n	%	n	%
Demography						
Male gender	440/525	83.8%	433/526	82.3%	873/1051	83.1%
Age (years, median, IQR)[1]	67.0	(58.0, 72.0)	66.0	(60.0, 73.0)	66.0	(59.0, 73.0)
BMI (median, IQR)[1]	28.10	(25.5, 31.0)	28.0	(25.3, 30.9)	28.1	(25.4, 31.0)
Medical history						
Renal impairment						
Normal (CC>85ml/min)	320/525	61.0%	324/526	61.6%	644/1051	61.3%
Moderate (CC>50 & <85)	178/525	33.9%	176/526	33.5%	354/1051	33.7%
Severe (CC<50)	24/525	4.6%	21/526	4.0%	45/1051	4.3%
Dialysis (regardless of CC)	3/525	0.6%	5/526	1.0%	8/1051	0.8%
Extracardiac arteriopathy	97/525	18.5%	96/526	18.3%	193/1051	18.4%
Active endocarditis	3/525	0.6%	2/526	0.4%	5/1051	0.5%
Poor mobility	23/525	4.4%	18/526	3.4%	41/1051	3.9%
Critical preoperative state	5/525	1.0%	7/526	1.3%	12/1051	1.1%
Previous cardiac surgery	5/525	1.0%	6/526	1.1%	11/1051	1.0%
Diabetes on insulin	98/525	18.7%	82/526	15.6%	180/1051	17.1%
Chronic pulmonary lung disease	56/525	10.7%	71/526	13.5%	127/1051	12.1%
NYHA						
I	136/525	25.9%	145/526	27.6%	281/1051	26.7%
II	272/525	51.8%	267/526	50.8%	539/1051	51.3%
III	107/525	20.4%	104/526	19.8%	211/1051	20.1%
IV	10/525	1.9%	10/526	1.9%	20/1051	1.9%
LV function						
Good (LVEF >50%)	366/525	69.7%	375/526	71.3%	741/1051	70.5%
Moderate (LVEF 31% - 50%)	145/525	27.6%	138/526	26.2%	283/1051	26.9%
Poor (LVEF 21% - 30%)	12/525	2.3%	12/526	2.3%	24/1051	2.3%
Very poor (LVEF <20%)	2/525	0.4%	1/526	0.2%	3/1051	0.3%
Recent MI	101/525	19.2%	98/526	18.6%	199/1051	18.9%
Pulmonary hypertension						
Moderate (PA systolic 31-55mmHg)	26/523	5.0%	30/526	5.7%	56/1049	5.3%
Severe (PA systolic >55mmHg)	4/523	0.8%	3/526	0.6%	7/1049	0.7%
None	493/523	94.3%	493/526	93.7%	986/1049	94.0%
EuroSCORE II (median, IQR)	1.25	(0.81, 2.08)	1.22	(0.84, 2.04)	1.24	(0.83, 2.05)
Diabetes	223/524	42.6%	188/526	35.7%	411/1050	39.1%
CVA/TIAs	33/524	6.3%	36/526	6.8%	69/1050	6.6%
Atrial fibrillation	25/524	4.8%	32/526	6.1%	57/1050	5.4%
Unstable angina	57/485	11.8%	61/492	12.4%	118/977	12.1%
Congestive heart failure	12/524	2.3%	10/526	1.9%	22/1050	2.1%
Preoperative medications						

	Randomised to CECC (n=536)		Randomised to MiECC (n=535)		Overall (n=1071)	
	n	%	n	%	n	%
Heparin (fractionated/ unfractionated)	134/524	25.6%	150/526	28.5%	284/1050	27.0%
Prophylactic	118/134	88.1%	128/150	85.3%	246/284	86.6%
Treatment	16/134	11.9%	22/150	14.7%	38/284	13.4%
Antiplatelet (P2Y12 inhibitors)	129/524	24.6%	131/526	24.9%	260/1050	24.8%
Warfarin	9/524	1.7%	4/526	0.8%	13/1050	1.2%
New oral anticoagulants	32/524	6.1%	31/526	5.9%	63/1050	6.0%
Aspirin Not P2Y12	268/368	72.8%	264/360	73.3%	532/728	73.1%
Haemoglobin (mean, SD)[1]	13.88	1.72	13.94	1.64	13.91	1.68
Platelets (mean, SD)[1]	239.88	73.43	235.81	70.17	237.84	71.81
Operative details						
Operation						
CABG	447/530	84.3%	449/532	84.4%	896/1062	84.4%
AVR	49/530	9.2%	48/532	9.0%	97/1062	9.1%
CABG + AVR	34/530	6.4%	35/532	6.6%	69/1062	6.5%
Operative priority						
Emergency	7/524	1.3%	3/523	0.6%	10/1047	1.0%
Elective	459/524	87.6%	453/523	86.6%	912/1047	87.1%
Urgent	58/524	11.1%	67/523	12.8%	125/1047	11.9%

[1] missing for 20 patients (11 randomised to CECC and 9 randomised to MiECC)

Table 2 Frequencies of primary and secondary outcomes.

	Randomised to CECC (n=536)		Randomised to MiECC (n=535)	
	n	%	N	%
Experienced a primary outcome event[2]	69/522	13.2%	50/517	9.7%
All-cause mortality	10/524	1.9%	8/522	1.5%
Any other SAE (not included in primary outcome)	68/509	13.4%	53/504	10.5%
Blood products used post-operatively				
Any red cell transfusion[3]	201/521	38.6%	168/518	32.4%
Units transfused intra-operatively				
1 unit transfused	52/521	10.0%	35/519	6.7%
2 units transfused	51/521	9.8%	24/519	4.6%
3+ units transfused	10/521	1.9%	3/519	0.6%
Units transfused post-operatively				
1 unit transfused	75/522	14.4%	62/520	11.9%
2 units transfused	52/522	10.0%	47/520	9.0%
3+ units transfused	29/522	5.6%	30/520	5.8%
Any other blood product transfusion[3]	55/521	10.6%	58/518	11.2%
Time to ICU discharge (hours) (median, IQR)[4]	23.95	(20.7, 69.0)	24.0	(21.0,67.0)
Time to hospital discharge (days) (median, IQR)[5]	7.0	(6.0, 8.0)	7.0	(6.0, 8.0)

[1] Treatment effects: RR=Risk ratio, HR=Hazard ratio

[2] ECGs were not available for suspected MIs and suspected MIs were confirmed (serum troponin >500 ng/L) for only 5 patients. Including all patients with a suspected MI only as having the primary outcome did not change the treatment effect (RR=0.77,95% CI 0.59, 1.00, p=0.048).

[3] The statistical analysis plan erroneously defined the transfusion outcomes as post-op transfusions only. The initial analysis shared with investigators used this definition. After seeing the transfusion percentages for intra- and post-op RBC transfusion and checking the definition in the protocol (which refers to any RBC transfusion) the SAP was corrected, the analysis code revised and the model re-run.

[4] missing for 34 patients (17 randomised to CECC and 17 to MiECC)

[5] missing for 25 patients (12 randomised to CECC and 13 to MiECC)

Table 3 Frequencies of serious adverse events (SAEs) not qualifying for the primary outcome in CECC and MiECC groups.

	Randomised to CECC (n=536)		Randomised to MiECC (n=535)		Overall (n=1071)	
	n/N	%	n/N	%	n/N	%
Any other SAE (not included in primary outcome)	68/509	13.4%	53/504	10.5%	121/1013	11.9%
Cardiac arrest	7/521	1.3%	6/517	1.2%	13/1038	1.3%
SVT/AF requiring treatment	9/521	1.7%	2/517	0.4%	11/1038	1.1%
VF/VT requiring intervention	1/521	0.2%	0/517	0.0%	1/1038	0.1%
New pacing	2/521	0.4%	2/517	0.4%	4/1038	0.4%
Vasopressors used	6/518	1.2%	4/514	0.8%	10/1032	1.0%
Any inotropes used[1]	4/520	0.8%	11/515	2.1%	15/1035	1.4%
IABP inserted	1/521	0.2%	1/517	0.2%	2/1038	0.2%
Pulmonary artery catheter inserted	0/520	0.0%	0/516	0.0%	0/1036	0.0%
Vasodilator used	8/521	1.5%	3/515	0.6%	11/1036	1.1%
Mask CPAP	4/521	0.8%	0/516	0.0%	4/1037	0.4%
ARDS	2/521	0.4%	1/516	0.2%	3/1037	0.3%
Pneumothorax or pleural effusion requiring drainage	3/521	0.6%	4/516	0.8%	7/1037	0.7%
Peptic ulcer/GI bleed/ perforation	0/520	0.0%	0/517	0.0%	0/1037	0.0%
Pancreatitis (amylase >1500iu)	0/520	0.0%	0/517	0.0%	0/1037	0.0%
Ischaemic bowel requiring treatment	1/520	0.2%	1/517	0.2%	2/1037	0.2%
Transient Ischaemic Attack (TIA)	2/520	0.4%	0/517	0.0%	2/1037	0.2%
Deep Vein Thrombosis (DVT)	0/520	0.0%	0/517	0.0%	0/1037	0.0%
Pulmonary embolus	0/520	0.0%	0/517	0.0%	0/1037	0.0%
Excess bleeding, not requiring re-operation	2/520	0.4%	5/516	1.0%	7/1036	0.7%
Pericardial effusion	2/520	0.4%	4/517	0.8%	6/1037	0.6%

[1] *1 patient with inotrope use SAE in MiECC group received the alternative treatment.*