

Minimal extracorporeal circulation: An appraisal from a private practice

Marius J. Swart* and Gina Joubert#

*Mediclinic Hospital, Bloemfontein and Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa.

#Department of Biostatistics, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa.

Address for correspondence:

Marius J. Swart
Suite 111
Mediclinic
Bloemfontein
9300
South Africa

Email:

mjswart@kfc.bfnmcc.co.za

INTRODUCTION

Cardiopulmonary bypass (CPB) and cardiac arrest allow the surgeon to perform controlled anastomoses during coronary artery bypass graft surgery (CABG). However, this comes at a cost. A systemic inflammatory response is a risk for organ damage and thus mortality and morbidity. Beating heart surgery, or off-pump CABG (OPCAB), was re-introduced to attenuate this effect. Many studies demonstrated very optimistic results in favour of OPCAB compared to CABG with conventional CPB. However, not everybody is convinced by the benefits, and this was addressed in a review on whether it would be beneficial to change to OPCAB.⁽¹⁾ In this study, the combined prevalence of mortality, myocardial infarction, stroke and new dialysis was 4%. To improve this with even 25% would require 10 600 patients, which is impossible in the average private cardiac practice in South Africa. Many randomised controlled studies could not demonstrate clear benefits and surgeons are losing interest in the OPCAB technique.⁽²⁾ This is confirmed by a review from the Cochrane Libraries. Based on the current evidence, CABG should be done with conventional CPB.⁽³⁾

A new CPB system has been developed. The argument is that minimal extracorporeal circulation (MECC or minibypass) should reduce the inflammatory response associated with conventional CPB.⁽⁴⁾ This system allows cardiac arrest, while maintaining the circulation. The lack of a venous reservoir with reduced priming volume, less cell trauma by the centrifugal pump driven by a magnet, and less blood-synthetic contact,

ABSTRACT

Introduction: The systemic inflammatory response associated with cardio-pulmonary bypass (CPB) is detrimental to organ function in varying degrees. Minimal extracorporeal circulation (MECC) assumes an attenuation of these deleterious effects. The aim of this study was to compare conventional CPB (CCPB) with MECC, in a population of patients who had their CABG done in a private practice in South Africa.

Methods: Two historical cohort analytical studies were done on patients who had isolated CABG done by one surgeon in the Mediclinic Bloemfontein. Patients who had their CABG done using CCPB were compared statistically using logistic regression to those who had their CABG done with MECC. A propensity score matching was also used to compare the 2 groups. In a second follow-up study, a once-off lactate on arrival in the intensive care unit was compared. A qualitative assessment of the technique by the various role-players in theatre was added to the initial study.

Results: The primary CCPB group had 1 572 patients. The MECC group comprised 367 patients. No statistically significant outcome difference was found in terms of mortality, major morbidity, post-operative blood loss or usage of homologous blood. Once the 2 groups were evenly matched, patients with MECC had a better serum creatinine postoperatively, but renal dialysis could not be avoided. Patients with MECC also had a statistically shorter hospital stay. The second study (CCPB n=63 and MECC n=100) confirmed the shorter hospital stay. There was no difference in the lactate value between the 2 groups. In general, there are varying levels of enthusiasm among the theatre specialists for a MECC strategy.

Conclusions: MECC protects the kidneys, but not so much against renal dialysis. MECC patients could stay for a somewhat shorter time in hospital. Tissue perfusion based on a once-off lactate level was equal. MECC might be technically more demanding. This article is an important addition to the literature that adds a local perspective. SAHeart 2019;16:22-27

all attribute to this possible beneficial effect. A reduction in markers of inflammation should result in reduced organ damage and therefore reduced postoperative complications.

“Evidence based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about care of individual patients”.⁽⁵⁾ The theoretical information regarding the beneficial effects of MECC, was thus introduced and applied in a private cardiac surgery practice.

The aim of this article was to report on 2 separate, but consecutive studies that were done to compare the effect of 2 CPB strategies in a population of patients who had their CABG done in a private practice. One study looked at the clinical outcome and a second study specifically compared a single blood-lactate level. These patients had their CABG done with either conventional cardiopulmonary bypass (CCPB) or minimal extracorporeal circulation (MECC). It is the clinical outcome that interests the surgeon, anaesthetist, referring cardiologist and obviously the patient. From a perfusion point of view, blood lactate is one way of verifying the adequacy of perfusion.⁽⁶⁾ Blood lactate of 4.0mmol/l or higher during CPB, is an indication of tissue hypoperfusion, and is associated with more postoperative complications.⁽⁷⁾

METHODS

Two historical cohort analytical studies were done. For the first study, all patients who had their isolated CABG done with cardiopulmonary bypass by 1 surgeon (MJS), in 1 hospital from 2000 - 2015, were included. Patients who required additional procedures were the only patients that were excluded. Conventional bypass (CCPB) was used from November 2000 until November 2011. In December 2011, all CCPB cases for CABG were switched to MECC. Again, all the patients operated on consecutively for isolated coronary artery disease until December 2015, were included. After December 2015, MECC was the CPB technique until July 2016.

The conventional bypass system used the Inspire[®] oxygenator and a roller pump (S5 Stöckert[®]). The priming solution was 2 500ml. The minisystem consisted of the Synergy[®] membrane oxygenator, a centrifugal cone driven by the heart lung machine (S5 Stöckert[®]), and a closed loop with surface treatment (PH.I S.I.O.®). The priming solution was 500ml. Activated clotting time was maintained above 400 seconds in both techniques. The standard myocardial protection was intermittent, antegrade, cold 1:1 blood:cardioplegia. Systemic temperature drifted down to 33 - 34°C, and patients were then actively rewarmed. Cell saving was used in every case.

These 2 groups of CCPB and MECC patients were compared regarding clinical outcomes using univariate analysis, stepwise logistic regression, and a propensity score matched analysis. Lastly, the experience of the various role-players in theatre was added as part of this clinical appraisal. This was done with a simple, subjective questionnaire about the overall experience with minibypass.

In the second study, CCBP was compared with MECC regarding a once-off lactate level on arrival in the intensive care unit (ICU). These procedures were done in the same institution by the same surgeon. The last 100 patients who had their CABG done with MECC (April 2015 until July 2016) and all the subsequent patients who had their CABG done again with CCBP (July 2016 until July 2017) were compared. The data of a number of patients in the MECC group were thus used in both studies.

Both studies were approved by the Health Sciences Research Ethics Committee of the University of the Free State (UFS). Individual patient consent was not obtained, as the names were not included in the database used by the researchers.

Basic demographic information was obtained from an existing, personal and ongoing data source. The clinical outcomes assessed were mortality at any time while in hospital and major morbidity (defined as re-exploration, stroke, prolonged ventilation, new renal dialysis, and sternal dehiscence). Other clinical outcomes included mediastinal drainage measured over 48 hours, homologous red blood cell replacement, a creatinine rise of 50% from a preoperative baseline, dialysis, and length of hospital stay (LOS). A fast-track approach was not applied with the change to MECC.

Blood lactate level was the primary outcome in the second study. A Siemens Rapidpoint 500 multi analyzer is permanently stationed in the ICU and this was used to do routine blood gas analysis, which included a lactate level. Although other surrogates for perfusion adequacy are routinely used, these were not documented for comparison. The 2 groups, CCPB and MECC, were once again compared regarding their EuroSCORE II, body surface area (BSA) and CPBtime (CPBt). CPBt and aortic cross clamp time were not available in the first study. Secondary outcomes compared, were mortality, morbidity and LOS. Serum creatinine was not evaluated again.

The Department of Biostatistics at the Faculty of Health Sciences of the University of the Free State did the statistical analysis. The results were summarised by frequencies and percentages (categorical variables), medians and means, and standard deviations or percentiles (numerical variables). Univariate analysis consisted of Mann-Whitney tests for numerical variables and chi squared or Fisher's exact tests for categorical variables. Stepwise logistic regression was performed to identify independent predictors of outcome. A propensity score matched analysis selected 367 CCPB patients to correspond with the MECC patients regarding age, diabetes mellitus, hypertension, body mass index, intra-aortic balloon pump, and Parsonette score.

RESULTS

Between November 2000 and November 2011, 1 572 patients had their isolated CABG done with CCPB. From December 2011 until December 2015, another 367 patients had MECC as a bypass technique. The statistical comparison is depicted in Table I. No significant differences were found in terms of mortality, morbidity and LOS. The CCPB patients had 46ml more mediastinal drainage over 48 hours compared to the MECC group. In both groups, 20% of patients required red blood cells from the blood bank. Acute kidney injury or a 50% rise in serum creatinine complicated 7.1% and 4.9%, respectively, in the CCPB and MECC groups (p=0.13). Some patients needed formal renal dialysis, 1.2% and 1.7% respectively (p=0.45).

It was clear that the basic demographic information of these 2 groups differed significantly (Table II). Therefore in the propensity score matched analysis, 367 patients from the CCPB group were evenly matched with the 367 patients who had their CABG done with MECC. The mean propensity scores in both groups were 0.29. Two significant differences in the

outcome were identified between these matched groups (Table III). A rise in creatinine was now more prominent in the CCPB groups, with 10.4% of the patients having a significant increase in postoperative serum creatinine compared to only 4.9% from the MECC group. The Odd Ratio (OR) for patients to develop a higher serum creatinine was 0.42 with the MECC (95% Confidence Interval [CI] 0.21;0.78). This was confirmed with the stepwise logistic regression, where MECC was shown to have a protective effect on the kidneys, but not to the point of limiting the number of patients who required dialysis. Parsonette score and pre-operative Chronic Kidney Disease III (CKDIII) predicted renal failure requiring dialysis. In the stepwise logistic regression, MECC did not contribute to any other commonly reported outcome – except for the more favourable serum creatinine post-operatively.

The second difference from a statistical point of view was the dissimilarity in LOS (Table III). CCPB patients stayed a mean of 6.4 days (median 5 days) and MECC patients 5.9 days (also a median 5 days). Although the medians are the same, there is some difference in the distributions. However, this difference in LOS was only when one compares percentage of patients who stayed longer than 6 days (CCPB 45.0% and MECC 36.3%). There was no difference in the 2 groups when the percentage of patients who stayed longer than 7 days (CCPB 21.3% and MECC 20.8%) was compared. The difference in LOS is probably, at most, half a day in favour of the MECC technique.

Two surgeons, 7 anaesthetists and 2 perfusionists answered a simple questionnaire to give information about their experience with MECC. All 11 specialists were aware of this bypass technique. One surgeon had a positive impression and 2

TABLE I: Outcomes of CCPB and MECC groups.

	CCPB n=1572	MECC n=367	P
Mortality	2.22%	2.45%	p=0.79
Morbidity	5.8%	5.7%	p=0.96
Mediastinal drainage (mean)	646ml	600ml	p=0.06
RBC	20%	19.3%	p=0.79
S-Creatinine	7.1%	4.9%	p=0.13
Dialysis	1.2%	1.7%	p=0.45
LOS (mean)	5.9 days	5.9 days	p=0.17

LOS = length of hospital stay, RBC = red blood cells, S = serum.

TABLE II: Pre-operative demographic information of CCPB and MECC groups.

	CCPB n=1572	MECC n=367	P
Age (median)	61	63	p<0.01
Diabetes mellitus	26%	34%	p<0.01
Hypertension	63%	69%	p=0.02
BMI	30.6	31.6	p<0.01
IABP	18%	26%	p<0.01
Parsonette (mean)	7.5	9.2	p<0.01

BMI = body mass index kg/m², IABP = intra-aortic balloon pump.

TABLE III: Outcomes of propensity score matched groups.

	CCPB n=367	MECC n=367	P
Mortality	3.54%	2.45%	p=0.39
Morbidity	7.1%	5.7%	p=0.43
Mediastinal drainage (mean)	611ml	600ml	p=0.69
Mediastinal drainage (median)	550ml	500ml	p=0.06
RBC	22.3%	19.3%	p=0.32
S-Creatinine	10.4%	4.9%	p<0.01
Dialysis	2.2%	1.7%	p=0.75
LOS (mean)	6.4 days	5.9 days	p=0.17
LOS (median)	5 days	5 days	p=0.02

LOS = length of hospital stay, RBC = red blood cells, S-Creatinine = a creatinine rise of 50% from a pre-operative baseline.

TABLE IV: Correlation with lactate levels (n=163).

	Correlation	P
EuroSCORE II	-0.05	P=0.55
BSA	0.22	p=0.01
CPBt	0.33	p<0.01
LOS	-0.01	p=0.85

BSA = body surface area m², CPBt = time, LOS = length of hospital stay, S-Creatinine = a creatinine rise of 50% from a pre-operative baseline.

TABLE V: Pre- and intra-operative comparisons in the lactate study.

	CCPB n=367		MECC n=367		P
	Mean	Median	Mean	Median	
EuroSCORE	2.73	1.41	3.93	1.89	0.31
BSA (m ²)	2.06	2.06	2.04	2.03	0.81
CPBt (minutes)	81.84	80	78.78	81	0.84

BSA = body surface area, CPBt = cardiopulmonary bypass time.

TABLE VI: Outcome comparisons in the lactate study.

	CCPB n=63	MECC n=100	P
Mortality (%)	1 (1.59)	1 (1)	p=1.00
Morbidity (%)	2 (3.17)	8 (8)	p=0.32
LOS (median days)	6	5	p=0.01
LOS (mean days)	7.6	6.5	P=0.01

LOS = length of hospital stay.

anaesthetists had a definite negative attitude toward mini-bypass. The other 8 specialists could not really determine a difference. One surgeon found MECC to be user-friendly, whereas 4 anaesthetists could not distinguish a difference. The rest (6 specialists) thought MECC was more challenging. At the time of the investigations, only 2 specialists would prefer to continue with MECC – 1 surgeon and 1 anaesthetist. Four anaesthetists felt unhappy about continuing with MECC. The rest (5 specialists) believed certain subgroups could benefit from MECC.

For the second study, 63 consecutive patients who had an isolated CABG done with CCPB (July 2016 until July 2017) were compared with the last 100 consecutive patients who had MECC (April 2015 until July 2016) as a bypass technique. The median lactate level on arrival in the ICU was 3.5mmol/l

(mean 4.11mmol/l) in the CCPB group and 3.6mmol/l (mean 4.03mmol/l) in the MECC group (p=0.84). As expected, lactate itself correlated, but only weakly (Spearman correlation coefficients), with BSA and CPB time, but not with the EuroSCORE II (Table IV). Lactate was not associated with death or major morbidity and did not correlate with LOS.

Although lactate level on arrival in the ICU was the primary outcome, other comparisons were again made. The 2 groups did not differ in terms of their EuroSCORE II, BSA and CPBt, with p values of 0.31, 0.81 and 0.84 respectively (Table V). As far as outcomes were concerned, no difference was seen in mortality or morbidity between the groups CCPB and MECC (Table VI). However, this second study confirmed the better LOS in patients who had their CABG done with MECC. The median LOS was 6 (7.6 mean) days and 5 (6.5 mean) days respectively (p=0.01 Mann-Whitney, 95%CI -1;0.0).

DISCUSSION

Since the start of this practice, by the end of 2000 CCPB was the CPB technique until December 2011. The CCPB technique was changed to MECC during December 2011 based on the advantages in the literature associated with MECC. A policy change was again introduced from July 2016 back to CCPB.

Apart from the combined numbers in review articles, this study is one of the larger, single institutional studies to compare CCPB with MECC.⁽⁸⁾ The fact that a reduction in the inflammatory response would result in less adverse effects associated with CPB, made sense.⁽⁹⁾ Unfortunately, the literature is not that convincing, and the clinical results are rather equivocal. This study's results are no different. Not only did the study by Svitek, et al. demonstrate no difference in the anti-inflammatory response, they also found no difference in the clinical outcome.⁽¹⁰⁾ Admittedly, it was a small study that involved only 54 patients. Another study showed improvement in inflammatory markers following MECC.⁽¹¹⁾ Larger studies seem to illustrate a difference in favour of MECC.⁽¹²⁾

At first glance, the impression is that this study would have a similar outcome to the 2 smaller studies mentioned. There was no difference in the common postoperative outcomes (Table I). However, this study confirmed the perception that patients have become, over time, a higher postoperative risk for mortality. Although the Parsonette score is no longer used to assess operative risk, it was still useful to demonstrate the change in patient demographics (Table II). Since the EuroSCORE changed in 2012 to an updated version (EuroSCORE II), Parsonette was applied in this first part of the study. It was considered to be inaccurate to use 2 different EuroSCOREs.

Once the 2 populations were comparable, 2 differences

became clear. Renal function and LOS seemed to be better with MECC (Table III). It was the serum creatinine that improved. MECC did not protect the kidneys enough to avoid dialysis. This observation is in line with Benedetto, et al.⁽¹³⁾ Their study was also a propensity score matched analysis. They used a different criterion to diagnose kidney injury, but still the incidence of kidney injury was reported as 42% vs. 29% (for CCPB and MECC respectively). Again, there was no difference in the prevalence of patients requiring renal dialysis. In their series, the OR for renal injury with MECC was 0.61 (95%CI 0.38;0.97), whereas the OR for renal impairment postoperatively in the local series was 0.42 (95% CI 0.21;0.78).

Although the LOS was initially similar, the MECC group stayed shorter (mean 5.9 days as opposed to 6.4 days), when the 2 population groups were evenly matched (Table III). It probably means that the higher risk (latter period) group (MECC) stayed the same number of days as the lesser risk (former period) group (CCPB) – but after the propensity score matching, the MECC patients stayed somewhat shorter. This half a day longer in hospital can probably be explained by the fact that more patients with CCPB had raised postoperative serum creatinine levels. A shorter LOS was also reported by Immer, et al.⁽¹⁴⁾ The LOS dropped from 9.3 days - 8.1 days with MECC. They did not however investigate postoperative renal function, except for the diuresis in the first 6 hours in the ICU, which was similar in the 2 bypass groups. In a large prospective study, no difference was seen in the LOS between CCPB and MECC patients.⁽¹⁵⁾ A slim improvement in LOS with MECC was reported by Wang.⁽¹⁶⁾ In their meta-analysis, the LOS in the 3 randomised trials was not statistically different, nor in the 2 cohort studies. However, the combination demonstrated a better LOS in favour of MECC, although it was only 18 hours.

Many studies report less mediastinal drainage and fewer units of red blood cells from a blood bank.⁽⁸⁾ This study could not however confirm this (Tables I and III). Post-operative drainage and red blood cell transfusion were also similar in the 2 groups in the study by Remedi. However, they reported a higher transfusion rate intra-operatively.⁽¹²⁾ Low homologous red blood cell consumption in this practice has been reported previously.⁽¹⁷⁾

Lactate is the conjugate base after lactic acid has lost a proton. This is the result of glucose and pyruvate metabolism in a hypoxic environment, but also when there is hypoperfusion of the liver as during CPB.⁽¹⁸⁾ In contrast to this study, Puehler and colleagues established a difference in the lactate on arrival in the ICU between CCPB and MECC patients.⁽¹⁵⁾ As a matter of interest, they found no difference between the lactate on arrival between MECC and OPCAB patients. They commented that the organ and tissue perfusion with MECC and OPCAB were better than with CCPB. They excluded patients in their series

with a body mass index (BMI) of $\geq 30\text{kg/m}^2$. In the local study, the mean BMI was $>30\text{kg/m}^2$ (Table II). This study demonstrated, as expected, a correlation between lactate and body surface area (BSA) and with CPBt (Table IV).

The fact that most of the in-theatre specialists were less enthusiastic about minibypass can be attributed to the technical challenges. The heart acts as the reservoir for blood volume and if too much blood is drained, the bypass circulation stops. A fuller heart makes distal anastomosis more challenging. The 2 specialists who were keen to continue with MECC were a surgeon who had the impression that renal function recovered more quickly with MECC, and an anaesthetist who wanted to get more experience with MECC. The other specialists had reservations about MECC as a bypass technique, although MECC might have a place for selected patients.

Any amount of air in the venous system will also bring the circulation to a standstill.⁽¹⁹⁾ The conventional system is much more forgiving.⁽²⁰⁾ The danger of air during true open-heart surgery is more real, and, therefore, as a local decision policy, no heart valve surgery with MECC was done. However, Baumbach, et al. and Wang, et al. reported a superior outcome of MECC in a population of valve surgery.^(21,16) It should also be borne in mind that with MECC there is no back-up of a cardiomy sucker to collect spilled blood in the chest back to the circulation. All blood gets sucked away to the cell saver, where plasma (clotting factors) and platelets are washed out. This could lead to coagulation pathology and more bleeding. Some studies report no MECC in redo cases.^(9,13) Among the 1 939 patients in the first study of the local series, 10.7% had a second or further sternotomy. No adverse effects related to bleeding or air were documented in the local series.

LIMITATIONS

Acute renal impairment after cardiac surgery is complex. Parolari, et al. found 15 predictors of post-operative acute kidney injury.⁽²²⁾ Recently, it was also reported that determining the pre-operative renal function reserve (RFR), even among patients with a normal glomerular filtration rate, could predict post-operative renal impairment.⁽²³⁾ Not all of these predictors were available in the local series.

Each patient's data are available in an existing and ongoing, self maintained Excel database. One person, the surgeon, collects this information and it is not audited by an independent person. Standard definitions are used, but they are still subjected to the surgeon's interpretation. Other variables are the number of anaesthetists and different perfusionists involved – each with his or her subtle differences in technique. The fact that the study was done over a long time span could also have had an influence on the outcomes. Larger numbers will always be preferred for

better statistical power. A randomised trial would however probably be a better way to compare. Yet, patients were not individually selected for a bypass technique – but followed the standing policy, which changed twice over 17 years. Hopefully the issue of non-randomisation was further addressed with the propensity score matching. A cost analysis was not done, but the MECC pack is about 6.5% more expensive than the CCPB pack.

CONCLUSIONS

From the first study, it was clear that patients are currently at a higher operative mortality risk than a decade or 2 ago. There was not much difference in the outcome between the 2 techniques, even if one compares exactly similar groups – as was done with the propensity score matched analysis. One can conclude that MECC protects the kidneys, but not to the point where dialysis is avoided. The positive consequence of this improved renal function, is that, statistically, patients with MECC stayed for a slightly shorter time in hospital. It furthermore seems that at the time of the first study, the different role-players in theatre were less enthusiastic about the MECC procedure. From the second study, it would appear that at least the tissue perfusion, as measured by the once off blood lactate, is not worse with MECC. MECC is a safe alternative in patients who could benefit from a bypass technique that is kinder to the kidneys.

This report does not necessarily contribute new information. The data from this study may be utilised to improve the power of future meta-analyses on this subject. Such a reflection is also important after application of information from elsewhere in a local context.

Conflict of interest: none declared.

REFERENCES

- Swart MJ, Joubert G. Should I change to OPCAB? *Cardiovasc J SA*. 2005;16:166-170.
- Briffa N. Off pump coronary artery bypass: A passing fad or ready for prime time? *Eur Heart J*. 2008;11:1346-49.
- Møller CH, Penninga L, Wetterslev J, et al. Off-pump versus on-pump coronary artery bypass grafting for ischaemic heart disease. *Cochrane Database of Systemic Reviews*. 2012;3: CD007224. DOI: 10.1002/14651858.CD007224.pub.2
- Vohra HA, Whistance R, Modi A, et al. The inflammatory response to miniaturised extracorporeal circulation: A review of the literature. *Mediators Inflamm*. 2009;2009:707042. DOI: 10.1155/2009/707042.
- Sackett DL, Rosenberg WMC, Gray JAM, et al. Evidence based medicine: What it is and what it isn't. *Br Med J*. 1996;312:71-2.
- Svenmarker S, Häggmark S, Ostman M. What is a normal lactate level during cardiopulmonary bypass? *Scand Cardiovasc J*. 2006;40(5):305-11.
- Demers P, Elkouri S, Martineau R, et al. Outcome with high blood lactate levels during cardiopulmonary bypass in adult cardiac operation. *Ann Thorac Surg*. 2000;70(6):2082-86.
- Alevizou A, Dunning J, Park JD. Can a mini-bypass circuit improve perfusion in cardiac surgery compared to conventional cardiopulmonary bypass? *Interactive Cardiovascular and Thoracic Surgery*. 2009;8:457-66.
- Immer FF, Ackermann A, Gygax E, et al. Minimal extracorporeal circulation is a promising technique for coronary artery bypass grafting. *Ann Thorac Surg*. 2007;84:1515-21.
- Svitek V, Lonsky V, Mandak J, et al. No clear clinical benefit of using mini-invasive extracorporeal circulation in coronary artery bypass grafting in low-risk patients. *Perfusion*. 2009;24(6):389-95.
- Beghi C, Nicolini F, Agostinelli A, et al. Mini-cardiopulmonary bypass system: Results of a prospective randomised study. *Ann Thorac Surg*. 2006; 81:1396-1400.
- Remadi JP, Rakotoarivelo Z, Marticho P, et al. Prospective randomised study comparing coronary artery bypass grafting with the new mini-extracorporeal circulation Jostra System or with a standard cardiopulmonary bypass. *Am Heart J*. 2006;151(1):198.e1-198.e7.
- Benedetto U, Luciani R, Goracci M, et al. Miniaturised cardiopulmonary bypass and acute kidney injury in coronary artery bypass graft surgery. *Ann Thorac Surg*. 2009;88:529-36.
- Immer FF, Pirovino C, Gygax E, et al. Minimal versus conventional cardiopulmonary bypass: Assessment of intraoperative myocardial damage in coronary bypass surgery. *Eur J Cardio-thoracic Surg*. 2005;28:701-704.
- Puehler T, Haneya A, Philipp A, et al. Minimal extracorporeal circulation: An alternative for on-pump and off-pump coronary revascularisation. *Ann Thorac Surg*. 2009;87:766-72.
- Wang C, Hua K, Yin L, et al. A meta-analysis of miniaturised versus conventional extracorporeal circulation in valve surgery. *Ann Thorac Surg*. 2016;102:2099-2108.
- Swart MJ, Joubert G, Van den Berg JA, et al. *Tabula viva chirurgi: A living surgical document*. *Cardiovasc J Afr*. 2016;27:170-6.
- Jabbari A, Banihashem N, Alijanpour E, et al. Serum lactate as a prognostic factor in coronary artery bypass graft operation by on pump method. *Caspian J Intern Med*. 2013;4(2):662-6.
- Curtis N, Vohra HA, Ohri SK. Mini extracorporeal circuit cardiopulmonary bypass system: A review. *Perfusion*. 2010;25(3):115-24.
- Baikoussis NG, Papakonstantinou NA, Apostolakis E. The "benefits" of the mini-extracorporeal circulation in the minimal invasive cardiac surgery era. *Journal of Cardiology*. 2014;63:391-6.
- Baumbach H, Rustenbach CJ, Ahad S, et al. Minimally invasive extracorporeal bypass in minimally invasive heart valve operations: A prospective randomised trial. *Ann Thorac Surg*. 2016;102:93-101.
- Parolari A, Pesce LL, Pacini D, et al. Risk factors for perioperative acute kidney injury after adult cardiac surgery: Role of perioperative management. *Ann Thoracic Surg*. 2012;93:584-91.
- Husain-Syed F, Ferrari F, Sharma A, et al. Preoperative renal functional reserve predicts risk of acute kidney injury after cardiac operation. *Ann Thorac Surg*. 2018;105:1094-1101.