INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH AND ANALYSIS

ISSN(print): 2643-9840, ISSN(online): 2643-9875

Volume 04 Issue 05 May 2021

DOI: 10.47191/ijmra/v4-i5-07, Impact Factor: 6.072

Page No.- 543-549

Long-Term Outcome Evaluation in Patient Undergoing Deep Hypothermic Circulatory Arrest in Aortic Arch Surgery

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Background: Aortic dissection is usually associated with low survival rates due to high prehospital and perioperative mortality, in addition with increased risk of postoperative complication in survivals. Since 1985, deep hypothermic circulatory arrest (DHCA) is often used in aortic arch surgery with main advantage to provide bloodless surgical field while protecting brain tissue during hypothermia. Nevertheless, it still raises concern of increasing neurologic sequelae and a potential decrease of long-term quality of life.

The aim of study: To evaluate the effect of DHCA used in aortic surgery on long-term quality of life.

Methods: In this observational case series we included a total of 24 patients who had aortic arch surgery requiring DHCA in the Pauls Stradins Clinical University Hospital Cardiac Surgery center, from January 2019 to December 2020. Seven patients were excluded due to intrahospital death. For the rest of the patients Quality of life (QOL) was evaluated using RAND SF36 questionnaire and MMSE test. Data regarding demographics, clinical characteristics, surgery type, duration of circulatory arrest, rectal and bladder temperatures were collected and analyzed using the SPSS 23 Statistics software IBM SPSS Statistics 21 (IBM Corporation, NY, USA). Statistical significance was assumed as two- tailed $p < 0.05$.

Results: A total of 17 patients were analyzed, we had 12 (71%) males and 5 (29%) females. A mean age was 60.71 (±13.8 SD) years, leading co-morbidity was hypertension – 11 (64.7%). There were 6 (35.3%) elective and 11 (64.7%) acute surgeries. Stan-ford A dissection (82.4%) constituted the main part of all cases. A 94.7% had aortic arch replacement. Most common postopera-tive complication was wound infection- 29.4%.

The mean cardiopulmonary bypass time, aortic cross-clamping and reperfusion time was 212 (±38.3, SD), 124 (±33.8, SD) and 70.2 (±32.9, SD) minutes, respectively. Core temperature during DHCA was 23.2 Cº (±3.2, SD) and a rewarming rate was 0.12 (±0.07, SD) Cº/min. No significance correlation between RAND SF36 questionnaire score (QoL questionnaire) and lowest DHCA temperature, aortic cross - clamping, reperfusion time, CPB time was observed, respectively - p=0.367, p=0.544, p=0.619, p=0. We found statistically significant moderate strength correlation between QOL and rewarming rate (r=0.550; p=0.022). Mean RAND SF36 questionnaire score was 71.9±10. and mean MMSE score was 27.9±5,3.

Conclusions: We found no correlation between quality of life and lowest temperature during surgery, aortic cross- clamping time, reperfusion time, however we found positive moderate strength correlation between rewarming rate and quality of life. Patient quality of life after surviving aortic arch surgery and deep hypothermic circulatory arrest compared to general healthy population quality of life is slightly reduced. Mini-mental state exam and RANDO short form health survey can be useful scoring system to evaluate patient quality of life.

INTRODUCTION

Aortic dissection (AoD) is among the most challenging cases for cardiac surgery team and requires numerous innovations in surgical and anesthesia care to ensure patient safety during surgery. Despite progressive experience with AoD management, it still presents a life threatening condition in cardiac surgery and can be rapidly fatal with 60% within the first 48 hours if not operated

(1-4) and is associated with increasing mortality over time. (5-15). Most cardiac surgical procedures can be accomplished by cardioplegia induced cardiac arrest and cardiopulmonary bypass (CPB) to maintain vital organ perfusion. In addition the surgical treatment of AoD necessitates complete cessation of circulation. While repairing an aortic arch, brain preservation is of the greatest concern during surgery. Therefore, organ protection, predominantly brain neuroprotection strategies, play important role. There are few neuroprotective strategies have been studied: deep hypothermic circulatory arrest (DHCA), retrograde cerebral perfusion (RCP) and antegrade cerebral perfusion (ACP). Hypothermia is the main method described of cerebral protection. DHCA is a technique that provides excellent surgery conditions while reducing organ ischaemia. Despite improvements in perioperative strategies with earlier diagnosis and immediate repair, mortality rates remains high - 8% - 15% after DHCA with stroke rates of 7 – 11% (16-18). There have been identified predictors of stroke after DHCA: duration of DHCA, increased age and atheroma or thrombi in the aorta. Patients after DHCA commonly suffer from long term cognitive dysfunction, particularly short and long term memory loss and information processing, therefore affecting patient quality of life. (20).

METHODS

In this observational case series we included a total of 24 patients who had aortic arch surgery requiring DHCA in the Pauls Stradins Clinical University Hospital Cardiac Surgery center, from January 2019 to December 2020. Seven patients were excluded due to intrahospital death. The Healthcare Associated Quality of life (HRQoL) interviews were performed during December 2020, 11(±9) months after surgery, using RAND-SF36 questionnaire and Mini mental state examination (MMSE) test. Each patient was contacted by phone. The RAND 36-Item Health Survey questionnaire was used in the interviews because it is one of the most widely used HRQoL evaluation instruments. The RAND-SF36 consists of an eight-dimensional questionnaire, with scores transformed to a 0- to 100-point scale, with higher scores denoting less limitations and problems in functioning. Measurements of RANDO SF36 can be seen in table 1.

Table 1. The RANDO-SF36

Measurements
Physical functioning (PF)
Physical-role (RP)
Bodily pain (BP)
Social functioning (SF)
General health (GH)
Emotional – role (RE)
Vitality (VT)
Mental health (MH)

Demographics, clinical characteristics (co-morbidities, blood pressure, type of pathology (Stanford A or B, brachyocephalic artery dissection)), surgery type (ascending aorta replacement, aortic arch replacement, aortic valve surgery), duration of circulatory arrest, mean cardiopulmonary bypass time (CPB), aortic cross-clamping and reperfusion time. Rectal and urinary bladder temperature were recorded. The standard neuroprotective protocol with methilprednisolone and thyopenthal as well as ACP was used. Endotracheal anesthesia is performed until CPB starts, then changed to total intravenous with thyopenthal and fentanyl 0.05 mkg/kg/min. The hematocrit level was held between 21-24% during operation. During deep hypothermia circulatory arrest near infrared spectrometry (NIRS) were used. After anesthesia department protocols the goal is to achieve core temperature - 25°C with 10 ml/kg/min antegrade cerebral perfusion.

All the data was analyzed using IBM SPSS Statistics 21 (IBM Corporation, NY, USA). The Kolmogorov–Smirnov test was used to check whether the variables followed a normal distribution. Normally distributed, continuous variables were presented as mean ± standard deviation (M ± SD) and categorical variables as percentages (%). In case values did not follow a normal distribution, the medians and interquartile ranges (IQRs) were presented. Odds ratios and 95% confidence intervals were calculated to evaluate factor impacts between groups. Comparisons between genotype groups were performed with Kruskal–Wallis H tests for nonparametric variables and with ANOVA for parametric variables. Pearson's x^2 correlation coefficient and p values were calculated, and Spearman's rank correlation coefficient was used where applicable. Statistical significance was assumed as two- tailed *p* <0.05. The study was approved by the Pauls Stradins University Hospital Ethics Committee.

RESULTS

A total of the 17 patients were included in the study, 12 (71%) male and 5 (29%) female. A mean age 60.7 (±13.8 SD) years. Leading co-morbidity was hypertension (64.7%). There were 11 (64.7%) emergency and 6 (35.3%) elective surgeries. Mostly there was Stanford A dissection (82.4%). 94.7% had aortic arch replacement.

Table 2. Group Characteristics

n = 17		
Demographics		
Age, median, y	60,7 ± 13,8	
Male gender, n (%)	12	(71 %)
Female gender, n (%)	5	(29 %)
Comorbidities, n (%)		
Chronic heart failure	11	(64)
Hypertension	13	(76)
Diabetes	2	(12)
Myocardial infarction	1	(6)
Pulmonary disease	3	(18)
Chronic kidney disease	2	(12)
Marphan's syndrome	1	(6)

The mean cardiopulmonary bypass time (CPB), aortic cross-clapming and reperfusion time was 212.0±38.3, 124.0±33.8 and 70.2±32.9 minutes, respectively. Core temperature during DHCA was 23.2±3.2 Cº. Rewarming rate was 0.12±0.07 Cº/min. The cardiac ICU stay varied between 2 to 10 days (± 4.7) and mean total in hospital stay was 11.5 days (7-28). Most common postoperative complication was operative wound infection- 29.4%.

Table 3. Perioperative characteristics

n = 17	
Perioperative data, n (±SD)	
Cardiopulmonary bypass time, s	212 ± 38,3
Aortic cross clamping, s	124 ± 33,8
Reperfusion time, s	70,2 ± 32,9
Core temperature, C°	23,2 ± 3,2
Rewarming rate, C°/min	0,12 ± 0,07

Table 3. Postoperative complications

n = 17		
Complications, n (%)		
Hemorrhagic event	4	(24)
Cardiac arrhythmia	2	(12)
Infection	6	(35)
Acute kidney injury	1	(6)

Mean RAND-SF36 results were slightly lower compared to the healthy reference population in physical functioning (75 vs 87), physical-role (76 vs 84), bodily pain(70 vs 78),social functioning(79 vs 84), general health(70 vs 72), emotional-role(81 vs 82), vitality(65 vs 69), but has a minor increase in mental health(75 vs 73). Mean cognitive result was 27.9±5.3 based on the results of MMSE, which in general shows no significant decrease cognitive functioning. Overall mean long term quality of life was 71.9±10.2%.

No significance correlation between RAND SF36 questionnaire score (QoL questionnaire) and lowest DHCA temperature, aortic cross - clamping, reperfusion time, CPB time was observed, respectively - p=0.367, p=0.544, p=0.619, p=0. We found statistically significant moderate strength correlation between QOL and rewarming rate (r=0.550; *p*=0.022).

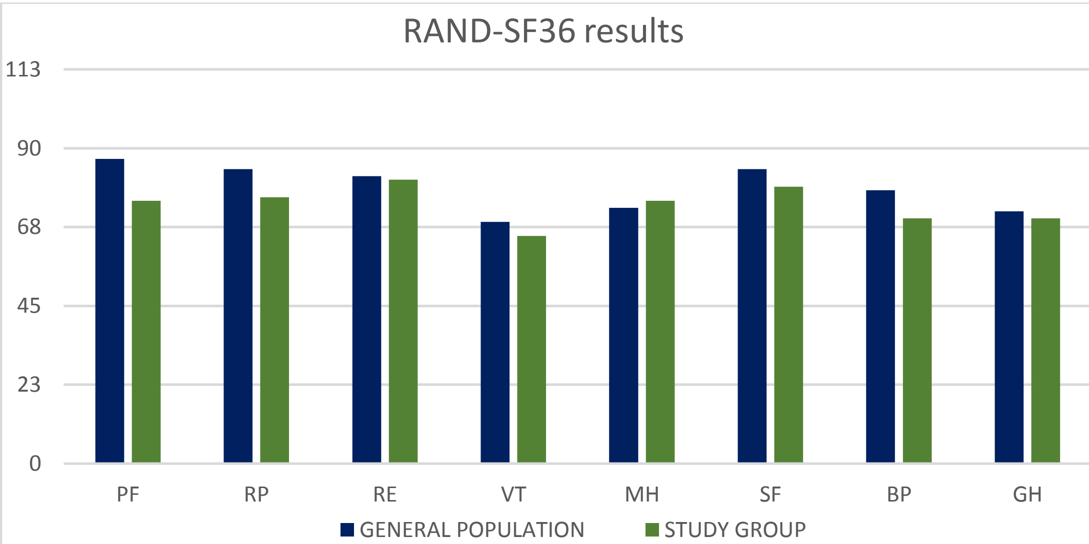

Table 1. Comparison of the RAND-36 results between general population and the study group.

DISCUSSION

Cerebral protection is an essential component of successful aortic surgery. Three main neuroprotection strategies are DHCA, RCP, ACP. DHCA was initially described in 1975 by Griepp (21), and it is still the main cerebral protection method during aortic arch surgeries. DHCA is a technique to provides excellent operating conditions while reducing organ ischemia. Cerebral metabolic rate for oxygen is related to brain temperature. Electrical activity of neuronal transmission of impulses and maintenance of cellular homeostasis are both supported by cerebral metabolism and temperature affects them. Hypothermia and general anaesthesia protect the brain against ischemia. At normothermia, brain injury occurs after around 4 min of circulatory arrest. Cerebral metabolism decreases by 6–7% for every 1°C decrease in temperature from 37°C. Therefore, brain cooling results in a reduction in oxygen requirements. Circulatory arrest is typically undertaken at 18 – 20°C and a range of safe periods for DHCA have been reported at this temperature. Most patients tolerate 30 min of DHCA without significant neurological dysfunction, but when this is extended to longer than 40 min, there is a marked increase in the incidence of brain injury. Above 60 min, the majority of patients will suffer irreversible brain injury, although there are still a small number of patients who can tolerate this although there are still a small number of patients who can tolerate this. (22-23) Surgical techniques such as selective ACP or RCP may be used to prolong the safe duration of DHCA. Both methods have advantages and disadvantages. Studies have shown that the main benefit of retrograde cerebral perfusion is the result of brain hypothermia and flushing air and debris off the brain circulation; however, it adds minimal perfusion to brain capillaries. (24-25) By contrast, ACP might lead to improved neurological outcomes because of a decrease in transcranial oxygen extraction when total body perfusion is reinstituted. (26, 27) ACP technique offers an almost unlimited safety period. However, the risk of embolisation is still high, especially in older patients with atherosclerotic vessels. It became clear that the gold strategy for neuroprotection is the combination of hypothermia with selective ACP. (28) On other hand hypothermia during CPB can be harmful. Depending on the body temperature and on the modalities of re-warming organ dysfunction like renal failure, impaired coagulation profile with increased bleeding, infection, postoperative shivering due to incomplete rewarming and 'after-drop' in body temperature or even rhabdomyolysis may occur. There is risk of brain hyperthermia during rewarming cold CPB. This rewarming period is associated with impaired cerebral oxygenation. (29) These periods of hyperthermia have been claimed to be responsible for 50–80% neurological injury and increase the risk of adverse neurological outcomes (30-31) Slow rewarming has been shown to decrease cerebral injury. (32) Despite improvements in surgical and anaesthetic techniques, peri-operative mortality (25%) and neurological complications (18%) remain high. (16-18) Furthermore, only 50% to 70% will be alive 5 years after surgery depending on age and underlying ethology. (33) Even perioperative mortality is high, quality of life and neurological outcome remains very important in this relative young group of patient. A few patients will recover without a major complication limiting quality of life, and few will be long-term survivors because of comorbid disease. Neurological complications are not rare 5% and 25%, and most importantly the rate of neurological complications is positively correlated with the patient's age and the duration of circulatory arrest. (34-35) Neuroprotective techniques are still a matter of interest in cardiac surgery, since CPB can cause neurological damage either by thromboembolism, hypoperfusion of watershed regions or inflammatory processes. Other neuroprotective strategies include pharmacological methods, glucose control, haemodilution, and acid-base management but there are no perfect neuroprotective techniques - harmless, easy manageable. Literature data suggest that permanent neurological deficits occurring after aorta surgery are mainly due to strokes caused by embolism rather than the direct effect of the cerebral protection method used. The most significant issue is the lack of accurate monitoring and control of brain temperature during CPB especially during rewarming. Temperature monitoring at two sites, typically the nasopharynx and bladder, is used to estimate brain and body temperatures, respectively. Studies have shown that bladder and tympanic temperatures correlate most closely with brain temperature. There is poor correlation between pulmonary artery catheter and rectal temperature measurements, and brain temperature. (36) The site that most closely reflects brain temperature is the jugular bulb. The addition of a temperature sensor to all jugular bulb catheters might allow more accurate monitoring. While world is searching for better cerebral protection technique, DHCA will be used. And while DHCA will be used, the question about neurological and cerebral perfusion monitoring techniques will rise. Right now neurological monitoring effect on outcome monitoring has limited evidence but still it is widely used in many centers. Generally, there are two categories of neurological monitoring that are used- monitors of cerebral substrate delivery (for example, transcranial Doppler sonography and near infrared spectroscopy (NIRS)) and monitors of cerebral function (for example quantitative electroencephalography (qEEG)). Balance between cerebral oxygen demand and its supply can be measured by the measurement of jugular venous oxygen saturation ($SjO2$). All these techniques are with limitations and not help guide and manage hypothermia and cerebral perfusion during aorta arch replacement. There is described a lot of techniques for brain protection. But there is lack of studies how these strategies effect patient quality of life. The RAND SF36 is one of the most widely used QoL evaluation instruments.

MMSE is widely used test for examination of cognitive function, which include attention, memory, language and orientation. MMSE and RANDO SF36 useful scoring system to evaluate patient qualty of life. While we are searching for better cerebral protection, we have to focus not only on short term goals but also on long term goals and patient quality of life. Our findings showed that patient quality of life after surviving aortic arch surgery and deep hypothermic circulatory arrest compared to general healthy population quality of life is slightly reduced.

CONCLUSIONS

We found no correlation between quality of life and lowest temperature during surgery, aortic cross- clamping time, reperfusion time, however we found positive moderate strength correlation between rewarming rate and quality of life. Patient quality of life after surviving aortic arch surgery and deep hypothermic circulatory arrest compared to general healthy population quality of life is slightly reduced. Mini-mental state exam and RANDO short form health survey can be useful scoring system to evaluate patient quality of life.

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