Journal of Medicine, Physiology and Biophysics
ISSN 2422-8427 An International Peer-reviewed Journal
Vol.48, 2018

Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery

Dr Faraz Shakoor[1] Dr Ayat Shakoor[1] Dr Muhammad Talha Ullah Khan[2] Muhammad Zeeshan[3]
1.House Officer Nishtar Hospital Multan
2.Medical Officer Basic Health Unit Aali Wala
3.Msc. Statistician BZU Multan

Abstract
Objective: To determine the effect of individualized blood pressure management targeted upon the physiology of individual patient could help in decreasing the risk postoperative organ dysfunction. **Methodology** It was a randomized trial carried out in department of general medicine from March 2016 to March 2017. An approval from Ethics committee was taken. An informed consent in the form of a written document was taken from every patient. Data was analyzed by using SPSS version 24. Student t-test and $\chi 2$ test that was unadjusted was performed for the analysis of primary outcome. P value ≤ 0.05 was considered as significant. **Results**: in the Individualized group, Primary composite outcome was noted as (36.7%) n=55. Acute kidney injury according to RIFLE criteria; Risk, injury and failure was observed as (17.3%) n=26, (9.3%) n=14 and (6%) n=9 respectively. Use of renal replacement therapy was noted as (8%) n=12. Acute heart failure occurred in (6%) n=9. respectively. For Standard treatment group, Primary composite outcome was noted as (48.7%) n=73. Use of renal replacement therapy was noted as (6.7%) n=10. Acute heart failure occurred in (1.3%) n=2. Need for noninvasive or invasive ventilation and sepsis was noted as (30.7%) n=46 and (18%) n=27 respectively. **Conclusion**: High Postoperative risk patients having major abdominal surgery, the mode of management directed towards the individual blood pressure as compared to standard mode of management proves to be fruitful in decreasing the risk for postoperative organ dysfunction.
Keywords: Blood Pressure, Organ Dysfunction, Postoperative complications, Sepsis.

Introduction

There is increasing rate of patients going through major surgery with increasing rate of improvement in the field of medicine[1]. Nonetheless, there is still a risk of morbidity and mortality among these patients due to complications that may arise during the surgery. one such complication is the hemodynamic imbalance[2]. It has been observed that hypotension during the surgery is related to insult to multiple critical organs such as brain, heart, and kidney and is associated with increased mortality among high-risk patients. Although, this hypotension is one of the avoidable element since arterial blood pressure can be altered with the use of IV fluids and vasopressin agents[3]. So far, no unanimity has been found on the debate of optimum blood pressure as a standard threshold for the optimal perfusion of these organs. At present, a decrease of "30-50% off of baseline, mean arterial pressure lower than 60mmHg, and systolic blood pressure of less than 80mmHg" is the standard threshold for the treatment in clinical practice depicting the defect in consensus[4,5]. Recent guides given by the American Heart Association and the American College of Cardiology encourage an individualized care for patients undergoing high-risk surgeries with comorbidities. Those patients already suffering from hypertension, having ill self-regulatory and feedback phenomenon of kidney and lungs are more prone to ischemia at lower levels of blood pressure[6,7]. Thence, high blood pressure targetted therapy to such patients may save the patients from grave risk. for critically ill patients, the consensus guide suggests adjusting blood pressure at premorbid levels. Nonetheless, there is lack of evidence for an individual strategy in the surgery[7,8]. This study has been carried out to establish if an individualized targetted therapy of systolic blood pressure accustomed to the patient's usual levels will be helpful in decreasing the likelihood of organ dysfunction in comparison to the customary practice[9,10].

Methodology

Study design: It was a randomized trial carried out in department of general medicine from March 2016 to March 2017. An approval from Ethics committee was taken. An informed consent in the form of a written document was taken from every patient. To review blinding and the study conduct, an autonomous committee was formed for the monitoring of safety.

Study Participants: The eligibility criteria included age above 50 years, surgery under general anesthesia of two hours or longer, having a risk of class 3 or more of acute kidney injury before the surgery, not meeting any exclusion criteria. The risk index for acute kidney injury varies 1 to 4, with 4 being at highest risk of acute kidney injury preoperatively. The exclusion criteria comprised of chronic kidney disease, acute coronary

syndrome, uncontrolled hypertension, decompensated heart failure, or receiving norepinephrine, or a part of another study.

Study Interventions: Patients classified in 1:1 to be given standardized or individualized therapy. Patients resting BP was gained from their medical records to be used as a reference level. In case of unavailability of the records, a nurse measured the blood pressure of the patient. For the patients in conventional treatment class IV, was given in 6mg bolus, as determined if there was a fall in systolic blood pressure from patient's standard measurement below 40% then 15. For the individual treatment class, systolic blood pressure was supposed to stay between ±10percent of the reference range by infusing norepinephrine continuously. It was diluted by addition of 0.9% saline in 250ml as 2.5mg. Both of the study groups received ringer lactate solution IV at 4ml/kg/hr to fulfill the fluid demand. To attain a maximum level of stroke volume, 6% hydroxyethyl starch in 0.9% saline was given as additional fluids according to the protocols of the hemodynamic log scale. For the patients in individual treatment class, a decrease in the levels of norepinephrine was suggested for the risk of bradycardia. Norepinephrine was allowed to use in the standard class of treatment when the systolic BP falls below the determined level after infusing a max dose of ephedrine, as a rescue treatment. The duration of intervention was from initiation of anesthesia to 4 hr after surgery. An attending physician was present at all times to scrutinize all the procedures according to the clinical criteria and practices. A catheter in radial artery was placed for continuous monitoring of BP in order to avoid unnecessary treatments.

Study Outcome: The primary outcome included systemic inflammatory reaction and one organ dysfunction at least. The organ systems were Respiratory (requiring ventilation for respiratory depression), renal (injury, risk, loss, failure or end-stage kidney disease) neurologic (stroke) CVS (cardiac failure). The frequency and acerbity of dysfunction of the organ were determined once every day at routine evaluation during follows up. The secondary results comprised of the discrete element of the primary outcome, post-op complications included sepsis, stroke, acute heart failure, and surgical complications such as infection, a leak of the anastomosis, reoperation. Major adverse effects were bleeding and bradycardia.

Blinding and Randomization: Data collection, randomization, and enrollment were done with the help of web-based system. Randomization was done by a minimization log while stratification was performed on the basis of need of surgery, site of surgery, site of study. Blinding was strictly done for the data collection and follow up. Similarly the post-op care was providing the medical team. Investigator, statisticians, safety monitoring and data collecting team had no information on group tasks. Verification of outcome was done as defined by the criteria designed by the principal investigator. The credibility limits and quality assurance among the data were checked automatically for validation. Data was scrutinized additionally and was verified.

Statistical Analysis: Data was analyzed by using SPSS version 24. Mean and SD were calculated for numerical variables like age, height, systolic and diasystolic blood pressure. Frequency and percentages were calculated for qualitative data like gender, ASA status, acute kidney injury, stroke, need of ventilation, sepsis, surgical complications. Student t-test and $\chi 2$ test that was unadjusted was performed for the analysis of primary outcome. P value ≤ 0.05 was considered as significant.

Results

A total number of 300 patients were enrolled in this study, both genders. The study patients were further divided into two equal groups i.e. individual treatment and standard treatment respectively. The mean age, height, systolic blood pressure, Diastolic blood pressure, Serum creatinine at inclusion, estimated GFR Overall mean, Among those with estimated GFR <60 of the individualized treatment patients' was 59.63±4.66 years, 165.13±2.58 cm, 135.97±7.19 mm Hg, 75.50±5.46 mm Hg, 0.94±0.31 mg/dL, 88.23±2.46 mL/min/1.73 m^2, 46.10±2.45 mL/min/1.73 m^2 respectively. There were (85.3%) n=128 males and (14.7%) n=22 females. ASA physical status classes II, III and ≥IV was noted as (46%) n=69, (50.7%) n=76 and (3.3%) n=5 respectively. Acute kidney injury risk index classes III, IV and V was noted as 55.3% n=83, (28%) n=42 and (16.7%) n=25 respectively. Chronic heart failure, Ischemic heart disease, renal impairment, Diabetes mellitus and Estimated GFR <60 mL/min/1.73 m2, No. (%) was (22%) n=33, (8.7%) n=13, (20%) n=30, (54.7%) n=82 and (16.7%) n=25 respectively. While, the mean age, height, systolic blood pressure, Diastolic blood pressure, Serum creatinine at inclusion, estimated GFR Overall mean, Among those with estimated GFR <60 of the standardardized treatment patients' was 62.51±6.36 years, 166.45±2.96 cm, 135.24±3.12 mm Hg, 77.90±1.96 mm Hg, 0.94±0.31 mg/dL, 87.63±2.18 mL/min/1.73 m^2, 50.90±5.74 mL/min/1.73 m^2 respectively. There were (80.7%) n=121 males and (19.3%) n=29 females. ASA physical status classes II, III and ≥IV was noted as (39.3%) n=59, (58%) n=87 and (2.7%) n=4 respectively. Acute kidney injury risk index classes III, IV and V was noted as (50%) n=75, (36.7%) n=55 and (13.3%) n=20 respectively. Chronic heart failure, Ischemic heart disease, Renal impairment, Diabetes mellitus and Estimated GFR <60 mL/min/1.73 m2, No. (%) was (28.7%) n=43, (21.3%) n=32, (10.7%) n=16, (48.7%) n=73 and (18.7%) n=28 respectively. The differences were statistically significant of age (p=0.000), height (p=0.000), diastolic blood pressure (p=0.000), ischemic heart

disease (p=0.002), renal impairment (p=0.025), estimated GFR overall mean (p=0.026) and among those with estimated GFR <60 mL/min/1.73 m^2 (p=0.000) with regards to groups. (Table. 1).

Primary composite outcome was noted as (36.7%) n=55. Acute kidney injury according to RIFLE criteria; Risk, injury and failure was observed as (17.3%) n=26, (9.3%) n=14 and (6%) n=9 respectively. Use of renal replacement therapy was noted as (8%) n=12. Acute heart failure occurred in (6%) n=9. Stroke occurred in (1.3%) n=2. Reintubation was observed as (13.3%) n=20. Need for noninvasive or invasive ventilation and sepsis was noted as (18%) n=27 and (9.3%) n=14 respectively. Use of renal replacement therapy was observed as (3.3%) n=5. Need for noninvasive or invasive ventilation, sepsis, acute heart failure, stroke, surgical site infection, surgical reoperation, anastomotic leakage was observed as (20.7%) n=31, (16%) n=24, (2.7%) n=4, (2%) n=3, (15.3%) n=23, (16.7%) n=25 and (19.3%) n=29 respectively. While, death at day 30 was occurred (6%) n=9 patients.

Primary composite outcome was noted as (48.7%) n=73. Acute kidney injury according to RIFLE criteria; Risk, injury and failure was observed as (27.3%) n=41, (14.7%) n=22 and (9.3%) n=14 respectively. Use of renal replacement therapy was noted as (6.7%) n=10. Acute heart failure occurred in (1.3%) n=2. Stroke occurred in (0.7%) n=1. Reintubation was observed as (12%) n=18. Need for noninvasive or invasive ventilation and sepsis was noted as (30.7%) n=46 and (18%) n=27 respectively. Use of renal replacement therapy was observed as (8%) n=12. Need for noninvasive or invasive ventilation, sepsis, acute heart failure, stroke, surgical site infection, surgical reoperation, anastomotic leakage was observed as (26%) n=39, (28%) n=42, (10.7%) n=16, (0.7%) n=1, (30.7%) n=46, (27.3%) n=41 and (15.3%) n=23 respectively. While, death at day 30 was occurred (6.7%) n=10 patients.

The differences were statistically significant of Primary composite outcome (p=0.036), risk (p=0.038), Need for noninvasive or invasive ventilation (p=0.011), sepsis (p=0.029). Whereas; the differences were also significant of sepsis (p=0.012), acute heart failure (p=0.005), Surgical site infection (p=0.002), Surgical reoperation (p=0.026). (Table. 2).

Table. 1
Baseline characteristics among both the groups

Characteristics	Individual treatment (n=150)	Standard treatment (n=150)	P Value
Age	59.63±4.66	62.51±6.36	**0.000**
Gender			
Male	(85.3%) n=128	(80.7%) n=121	**0.282**
Female	(14.7%) n=22	(19.3%) n=29	
Height cm	165.13±2.58	166.45±2.96	**0.000**
ASA physical status class			
II	(46%) n=69	(39.3%) n=59	**0.442**
III	(50.7%) n=76	(58%) n=87	
≥IV	(3.3%) n=5	(2.7%) n=4	
Acute kidney injury risk index class			
III	55.3% n=83	(50%) n=75	**0.259**
IV	(28%) n=42	(36.7%) n=55	
V	(16.7%) n=25	(13.3%) n=20	
Reference blood pressure, mm Hg			
Systolic	135.97±7.19	135.24±3.12	**0.258**
Diastolic	75.50±5.46	77.90±1.96	**0.000**
Preexisting conditions			
Chronic heart failure	(22%) n=33	(28.7%) n=43	**0.184**
Ischemic heart disease	(8.7%) n=13	(21.3%) n=32	**0.002**
Renal impairment	(20%) n=30	(10.7%) n=16	**0.025**
Diabetes mellitus	(54.7%) n=82	(48.7%) n=73	**0.298**
Serum creatinine at inclusion, mean (SD), mg/dL	0.94±0.31	0.94±0.31	**1.0**
Estimated GFR			
Overall, mean, mL/min/1.73 m^2	88.23±2.46	87.63±2.18	**0.026**
Among those with estimated GFR <60 mL/min/1.73 m^2, mL/min/1.73 m^2	46.10±2.45	50.90±5.74	**t0.000**
Estimated GFR <60 mL/min/1.73 m^2	(16.7%) n=25	(18.7%) n=28	**0.650**

Table. 2
Distribution of Primary and Secondary Outcomes among the Groups

Characteristics	Individual treatment (n=150)	Standard treatment (n=150)	P Value
Primary Outcome			
Primary composite outcome	(36.7%) n=55	(48.7%) n=73	**0.036**
Secondary Outcome			
Complications within 7 days			
Acute kidney injury according to RIFLE criteria			
Risk	(17.3%) n=26	(27.3%) n=41	**0.038**
Injury	(9.3%) n=14	(14.7%) n=22	**0.155**
Failure	(6%) n=9	(9.3%) n=14	**0.278**
Use of renal replacement therapy	(8%) n=12	(6.7%) n=10	**0.658**
Acute heart failure	(6%) n=9	(1.3%) n=2	**0.032**
Stroke	(1.3%) n=2	(0.7%) n=1	**0.562**
Reintubation	(13.3%) n=20	(12%) n=18	**0.728**
Need for noninvasive or invasive ventilation	(18%) n=27	(30.7%) n=46	**0.011**
Sepsis	(9.3%) n=14	(18%) n=27	**0.029**
Complications within 30 days			
Use of renal replacement therapy	(3.3%) n=5	(8%) n=12	**0.080**
Need for noninvasive or invasive ventilation	(20.7%) n=31	(26%) n=39	**0.275**
Sepsis	(16%) n=24	(28%) n=42	**0.012**
Acute heart failure	(2.7%) n=4	(10.7%) n=16	**0.005**
Stroke	(2%) n=3	(0.7%) n=1	**0.314**
Surgical complications			
Surgical site infection	(15.3%) n=23	(30.7%) n=46	**0.002**
Surgical reoperation	(16.7%) n=25	(27.3%) n=41	**0.026**
Anastomotic leakage	(19.3%) n=29	(15.3%) n=23	**0.360**
Death at day 30	(6%) n=9	(6.7%) n=10	**0.813**

Discussion

For every surgery and every procedure, there are certain complications and the risks that come along with them. But for every complication is a cure. As said by Pelosi P et al [11], "Good things come in threes: prevention, early recognition, and treatment " this is true for all the complicated cases and the risks associated with surgery endangering organ and system dysfunction. If these three simple steps are properly looked upon, patients can be saved from grave difficulties. These steps include identifying high-risk patients; prevent adverse effects from occurring and early apprehension and immediate treatment of the complexities that arise as a result of surgery either within the duration of surgery or after that. It can rescue the crisis of organ dysfunction or failure as a complication and hence mortality and morbidity rates can be declined. For this purpose, an individual strategy must be applied to all these components keeping in view the physiologic processes.

An appropriate knowledge of circulatory physiology plays a vital role in the prevention of complications, says Green [12]. A drawback of improper understanding has led to the development of interventions such as flow monitoring. It has been observed that they lead to fluid and sodium overload. This is of significant importance for patients having high risk. the increasing number of these patients has made it necessary for re-evaluating the eduction upon circulatory physiology and its management. It is advised to use multimodal therapy for achieving the maximum benefits and decreasing morbidity and complications.

Maintenance of vitals during a surgery is a crucial task. Such as control of hemodynamics. Labufeb L et al [13] claims that it initiates with the identification of patients having high risks. This delamination is required to determine the treatment of choice for control of hemodynamics bringing together the use of minimally invasive methods. the main target of hemodynamic approach is to attain a harmony between supply and demand of oxygen. Stroke volume is greatly affected by volume replacement on the basis of fluid titration. If the microcirculatory system is working optimally it's the best assurance of achieving the target. Similarly, Vincent J et al [14] found out that monitoring of CVS is crucial in maintaining the period hemodynamics. It has been observed that more than the use of devices, the correct interpretation of cardiac variables hs proved to be fruitful in saving the life of patients and preventing complications. For this purpose individual systems in the body must be paid appropriate attention according to the need and status of patients before starting the surgery keeping in view the complications and risk factors. Multiple variables must be integrated to achieve this goal. The physician

must be aware of interpretations and outcomes of all the" tools and parameters used in perioperative care".

For the above-mentioned purpose, the concept of goal-directed therapy is worth considering. There are multiple advantages of GDT over conventional fluid therapy in patients of cardiac surgery as seen by Li P et al [15] it brings about a significant reduction in the duration of hospital stay, morbidity, and mortality. The shorter duration of hospital shows that optimal ranges of hemodynamics improve the post-op recovery. Similar results have been demonstrated in a study by R. Makaryus et al [16] a decrease in LOS as well as multiple complications is seen after the application of goal-directed therapy. It has also been observed that early oral hydration after the surgery causes rapid remedial and rehabilitation after surgery. It is advised to keep the levels of IV Fluids to the least level and it should be independent of urinary output. Elaboration of "perioperative fluid management" must be done to recuperate tissue oxygenation, wound healing, pulmonary function, and GIT motility. Analogous results have been achieved in the study by Osawa EA et al [17]. They observed the GDT including the use if blood transfusions, fluids, and inotropes after a cardiac surgery in high-risk patients decreased the likelihood of 30-day morbidity and main complications. GDT reduces the rate of complication by 11%. As well as, decreases the length of hospital stay and postoperative mortality.

The GDT for fluids improves the results by an individual approach such as oxygen level management with the help of IV fluid administration and vasoactive infusions Manning M et al [18]. GDP has shown improvements over the conventional excessive administration of fluid. But it didn't demonstrate any aberrations when a comparison was made with restrictive therapy and extreme protocols for recovery. Although postop hypotension management is disputatious, it includes a mi of vasopressors, IV fluid, and other agents and methods. Excessive salt administration is advised to be restrained from.

A study conducted by Aronson S et al [19] has shown that perioperative blood pressure is directly related to the outcomes whereas it is hard to establish if untreated intraop hypotension or treated hypotension (with IV fluids or vasopressors) affects the outcomes as such. Although it is seen that every patient has his own "personalized signature of an acceptable low intraoperative BP" on the basis of his baseline blood pressure. In accordance with this statement, Futier E et al [20] found out that patients having abdominal surgery with high postoperative risk, postoperative organ dysfunction can be prevented by focusing on the management of individual therapy against SBP rather than accustomed standard therapy.

Conclusion

High Postoperative risk patients having major abdominal surgery, the mode of managment directed towards the individual blood pressure as compared to standard mode of managment proves to be fruitful in decreasing the risk for postoperative organ dysfunction.

Refrences

1. Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, et al.2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. J Nucl Cardiol. 2015;22(1):162-215.
2. Palmer BF. Renal dysfunction complicating the treatment of hypertension. N Engl J Med. 2002;347(16):1256-1261.
3. vanWaes JA, van KleiWA, Wijeysundera DN, vanWolfswinkel L, Lindsay TF, BeattieWS.
Association between intraoperative hypotension and myocardial injury after vascular surgery.Anesthesiology. 2016;124(1):35-44.
4. Haynes AB1, Weiser TG, Berry WR, Lipsitz SR, Breizat AH, Dellinger EP, et al; Safe Surgery Saves Lives Study Group. A surgical safetychecklist to reduce morbidity and mortality in a global population. N Engl J Med. 2009;360(5):491-499.
5.Devereaux PJ, Mrkobrada M, Sessler DI, Leslie K, Alonso-Coello P, Kurz A, et al; POISE-2 Investigators. Clonidine in patients undergoing noncardiac surgery. N Engl J Med. 2014;370(16):1504-1513.
6.Walsh M, Devereaux PJ, Garg AX, Kurz A, Turan A, Rodseth RN, et al. Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. Anesthesiology. 2013;119(3):507-515.
7. Sun LY, Wijeysundera DN, Tait GA, BeattieWS. Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. Anesthesiology. 2015;123(3):515-523.
8. Botto F, Alonso-Coello P, Chan MT, Villar JC, Xavier D, Srinathan S, et al. Vascular Events in Noncardiac Surgery Patients Cohort Evaluation (VISION)Writing Group. Myocardial injury after noncardiac surgery: a large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. Anesthesiology. 2014;120(3):564-578
9.Forouzanfar MH, Liu P, Roth GA. Global burden of hypertension and systolic blood pressure of at least 110 to 115mmHg, 1990-2015. JAMA. 2017;317(2):165-182.

10. Corcoran T ,Joy E, Rhodes J, Clarke S, Myles PS. Perioperative fluid management strategies in major surgery. Anesth Analg. 2012;114:640–651
11.Pelosi P, Abreu M. Good things come in threes: prevention, early recognition and treatment of organ dysfunction to improve postoperative outcome. Curr Opin Crit Care. 2016;22(4):354-6.
12. Green D. Role of Multimodal Monitoring (MMM) in the Perioperative Period: Improving Outcomes in High Risk Surgical Patients. 2016; 271-300.
13. Lebuffe G, Lazkani A. Post-operative consequences of hemodynamic optimization J Visc Surg. 2016; 153(6): S5-S9.
14. Vincent J, Pearse R, Payen D, Perel A, Hoeft A, Romagnoli S, et al. Perioperative cardiovascular monitoring of high-risk patients: a consensus of 12. Critical Care. Crit Care. 2015 8;19:224
15. Li P, Qu LP, Qi D, Wang YM, Shen B, Jiang WH, et al.Significance of perioperative goal-directed hemodynamic approach in preventing postoperative complications in patients after cardiac surgery: a meta-analysis and systematic review. Ann Med. 2017;49(4):343-351.
16. R. Makaryus, T.E. Miller, T.J. Gan. Current concepts of fluid management in enhanced recovery pathways.Br J Anaesth. 2018;120(2):376-383
17. Osawa EA, Rodes A, Landon G, Galas FR, Park CH, Almeida JP et al. Effect of Perioperative Goal-Directed Hemodynamic Resuscitation Therapy on Outcomes Following Cardiac Surgery: A Randomized Clinical Trial and Systematic Review. Crit Care Med. 2016;44(4):724-33.
18. Manning M, Dunkman W, Miller T. Perioperative fluid and hemodynamic management within an enhanced recovery pathway. J Surg Oncol. 2017;116(5):592-600.
19. Aronson S, Mythen M. Perioperative Management of High-Risk Patients Going Beyond “Avoid Hypoxia and Hypotension”. JAMA. 2017;318(14):1330-1332
20. Futier E, Lefrant J, Guinot P, Godet T, Lorne E, Cuvillon P et al. Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction
21. Among High-Risk Patients Undergoing Major Surgery A Randomized Clinical Trial. JAMA. 2017;318(14):1346-1357.