Clinical Case Reports

CASE REPORT

Is mean arterial pressure the best parameter in ischemic stroke?

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Key Clinical Message

This case series of 27 patients with large stroke challenges the current state of the art guiding hemodynamic management by blood pressure levels. The results show that assumed correlations of blood pressure, cardiac output, and systemic vascular resistance do not exist. Therefore, hemodynamic therapy may better be guided by cardiac output.

Keywords

Neurointensive care, Stroke.

Background

In ischemic stroke, the main hemodynamic target for acute therapy focuses on restoring and optimizing the penumbral perfusion [1]. With or without acute recanalization measures [1] MAP (mean arterial blood pressure) is used as a standard target parameter for improving CP (cerebral perfusion) being a readily accessible monitoring parameter on one side as well as its expected relation to CP due to vascular autoregulation of the brain and perfusion pressure on the other [2,3].

Mean arterial blood pressure results from a product of CO (cardiac output) and total SVR (systemic vascular resistance) [4], hence MAP is expected to correlate with CO. In case of insufficient MAP fluids are administered based on the Frank Starling-principle: the increase in preload leads to a larger CO until stroke volumes become constant with optimal preload. In case of insufficient result vasopressors are used [5]. Former studies have shown that MAP levels' correlations to CO hold true only during isovolemic state [4,5]. Furthermore, it has been shown that CO has a linear relationship with organ perfusion [6]. CO might therefore be a relevant parameter to increase penumbral perfusion in patients with ischemic stroke.

Methods

Patients admitted to the Neurological Intensive Care Unit of University Hospital Freiburg during 2008 and 2013 who were diagnosed with large ischemic stroke of the MCA (middle cerebral artery) territory via CT or MRI and underwent hemicraniectomy and hypothermia treatment were included in this prospective observational study. The patients included received advanced cardiac monitoring with a Vigileo or PiCCO system (Pulsion or Flotrack-System, Edwards Life, Irvine, California, United States of America) according to the in house-monitoring protocol. Advanced monitoring was used in addition to standard monitoring of MAP in patients with the following characteristics: (1) ischemic stroke >30% of the middle artery territory; (2) hemicraniectomy or hypothermia treatment; (3) impaired cardiac function (e.g., due to cardiomyopathy, acute myocardial infarction); (4) conditions effecting cardiac function due to metabolic changes (e.g., patients with subarachnoid hemorrhages); and (5) severe infections. Those systems perform an analysis of the arterial pulse contour and calculate a CI (Cardiac Index; index results from CO and stroke volume related to body surface) [4]. The PiCCO system additionally calculates a SVRI (SVR-index) among other parameters.

We assessed basal mean MAP-, CI-, and SVRI-levels, hemodynamic medication, their effect on hemodynamic parameters and time needed to accomplish aimed normal cardiac index levels of >3 and <5. Normal MAP was stated at >80 mmHg due to aimed CP pressure of 70 mmHg and assumed normal intracranial pressure of 10 mmHg. Fluid replacement or catecholamine administration (noradrenaline or dobutamine) was carried out in order to achieve normal levels of MAP and CI.

Statistical analysis was performed with Student's *t*-test or signed rank-test according to distribution level. A Spearman's analysis was carried out to calculate correlation of MAP and CI parameters at start and end of monitoring, at point of normal MAP and after optimizing treatment. Furthermore, correlations of SVRI-, MAP-, and CI-parameters were calculated.

Results

We included 27 patients (19 male, eight female, aged 19–77 years). Mean score of NIHSS (National Institute of Health-Stroke Scale) at hospital admission was 17.1 (±5.8) and of mRS (modified Rankin Scale) 4.8 (±0.6). NIHSS at discharge was 16.7 (±7.7) and mRS 5.1 (±0.6), respectively. Four patients had died.

Monitoring was performed via Vigileo (nine patients) and PiCCO system (18 patients). One received Vigileo monitoring after failure of the PiCCO system. Initial measure to increase MAP and CI was fluid replacement: colloids (916 ± 801 ml in six patients), crystalloids (836 ± 474 mL in 11 patients), erythrocytes (in case of hemoglobin <7 mg/dL; 750 ± 212 mL in two patients), or albumin (in case of albumin <2.0 g/dL; 200 mL in one patient). Furthermore, catecholamines, noradrenaline (0.57 μg/min ± 0.49 μg/min in 23 patients), or dobutamine (15 mg/min ± 9.3 mg/min in 13 patients), were administered. In seven patients, the noradrenaline dose was reduced from 0.44 μg/min (±0.27) to 0.23 μg/min (±0.21), in one patient dobutamine was reduced from 10 mg/min to 7.5 mg/min. Five patients did not need a change in treatment with ongoing noradrenaline treatment of 0.58 μg/min (±0.35) and dobutamine administration with 10 mg/min (±7.9). The mean time to accomplish normal CI was 6 h (±6 h), MAP then was 90.4 mmHg (±12.6). The effects of treatment are shown in Table 1. Target values for MAP was accomplished 92.2% (±10.4) and for CI was 82.9% (20.1) of the time.

Spearman's correlation analysis showed no correlation of MAP and CI levels ($r = 0.1$) with a significance level of $P < 0.01$ throughout the entire study period (Fig. 1). Neither did the two parameters correlate in the beginning of monitoring ($r = -0.229$, $P = 0.251$) nor at the end ($r = -0.105$, $P = 0.603$). No correlation could be detected

at normal MAP levels ($r = -0.199$, $P = 0.319$) or at normal CI levels ($r = -0.229$, $P = 0.251$). SVRI-values of patients with PiCCO monitoring revealed little correlation of SVRI and MAP ($r = 0.3$, $P < 0.0001$), but a significantly negative correlation of SVRI and CI ($r = -0.8$, $P < 0.0001$; Fig. 1).

Discussion

Our results challenge the current state of the art guiding hemodynamic therapy by MAP-levels since they show no correlation of MAP, CO and SVRI.

Up to date, hemodynamic therapy is adjusted according to MAP-levels. Former studies have shown that BP (blood pressure) levels influence neurological outcome: Leonardi-Bee et al. [7] describe a u-shaped relationship with higher risks of death with BP <150 mmHg or >150 mmHg in acute ischemic stroke, with a greater negative effect of hypotensive BP. Furthermore, BP <140 mmHg in patients receiving acute endovascular recanalization was a negative predictor for a poor neurological outcome [8,9]. In the long-term a low BP might have a negative effect on neurological functions [10].

Furthermore, it has long been established that MAP is a product of CO and SVR; correlations of these parameters are expected. Greater CO results from increased preload until optimal preload levels lead to a constant CO. According to the Frank Starling-principle preload and vascular resistance should therefore be optimized [4,5].

However, we were able to demonstrate that levels of CI and MAP do not correlate, regardless of increasing preload via volume administration or SVRI via noradrenaline therapy. Furthermore, we could demonstrate that MAP and SVRI correlate little only, whereas CI and SVRI show a negative relationship.

As optimal penumbral perfusion is targeted to reduce the final infarction volume [1], CP, dependent on cerebral perfusion pressure in regions with impaired autoregulation, needs to be adapted [2,11]. Systemic hemodynamics affecting CP are therefore essential for the penumbral perfusion.

Our data show that both hemodynamic monitoring and therapy are clinically important in order to increase CI, since it has been shown that they reduce the length of the stay on intensive care units [12]. The effects of hemodynamic treatments are similar to other studies [13]; in other studies lower dosages of catecholamines were applied [14,15]; targeted MAP levels were accomplished to 92% of monitoring time.

As we and others could show that MAP-levels do not necessarily correlate with CI and secondary CP due to its dependence on volume state CI levels might be a better target in order to optimize CP. Some studies did not

Table 1. Effects of treatment on MAP and CI levels.

	Basal levels of MAP (mmHg)	MAP (mmHg) at normal CI	Significance (MAP)	Basal levels of CI	CI after treatment	Significance (CI)
Baseline parameters	91.4 (±11.7)			3.0 (±0.9)		
Volume infusion, n = 11	96.4 (±15.6)	90.7 (±9.6)	P = 0.4	2.6 (±0.8)	3.7 (±0.8)	P = 0.08
Noradrenaline administration, n = 1	91	110		2.9	3.0	
Dobutamine administration n = 11	93 (±8.6)	88.9 (±10.8)	P = 0.4	2.7 (±0.7)	3.4 (±0.8)	P < 0.01
Reduction in noradrenaline dosage, n = 2	85.6 (±6.7)	92.8 (±21.1)	P = 0.4	3 (±0.6)	4 (±0.6)	P = 0.03

Mean levels (standard distribution) of MAP (mean arterial pressure) and CI (cardiac index) levels. Level of significance $P < 0.05$.
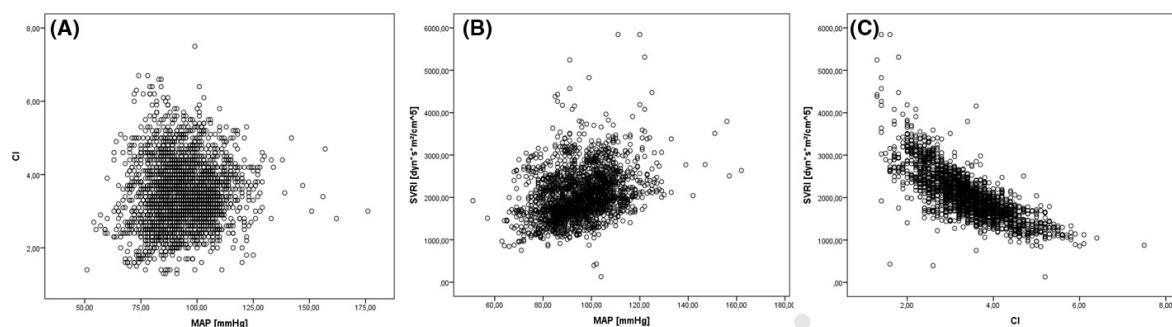
Figure 1. Correlation analyses of CI (cardiac index), MAP (mean arterial blood pressure), and SVRI (systemic vascular index).

detect a correlation of CI and CP [11], whereas others show that elevated CI increases CP: partial aortic occlusion in pigs [16] and passive leg raising lead to a significant higher CP due to shifting of blood volume [5]. Extending CI apart from MAP-levels via volume extension by albumin or hydroxyethyl starch solution in healthy men or sepsis-patients improves CP [17]. In monkeys with MCA-occlusion, cerebral blood flow increased by volume-guided augmentation of CI, independently of MAP-changes [18]. In a case report by Duke et al. [15] hyperdynamic therapy with increasing CO >8 by dobutamine (5–20 µg/kg/min) and albumin infusion lead to a normal neurological exam after 6 months in a formerly hemiplegic and severe aphasic patient. Similar results were found in patients with SAH (subarachnoid hemorrhage) when hyperdynamic therapy (albumin and dobutamine treatment 5–10 µg/kg/h) could reverse ischemic symptoms [14]. In accordance with these results SAH-patients with poor cardiac function were more likely than patients with good cardiac function to experience infarction due to vasospasms [19]. Furthermore, it could be shown that optimizing hemodynamic parameters (preload, CI) effects a better outcome [20,21]. Furthermore, optimizing CI lead to an improvement of CP [13].

Changes in hemodynamics following catecholamine use in our patients may vary: using vasopressors in patients with insufficient preload and in patients with pre-existing left ventricular insufficiency enhancement of

MAP may lead to reduced CI [5]. Patients with atrial fibrillation or beta blocker-treatment show a limited potential to increase CI and secondary CP [6]. As stroke patients often suffer from cardiac diseases the indirect effect on CP needs to be assessed in further investigations.

The results of our study are limited by the number of patients included. As others show a CI-dependent change in CP we expect to apply this for the penumbral region in patients with large stroke. This and its clinical benefit need to be proven in further clinical trials.

Acknowledgments

Conflict of Interest

None declared.

References

1. Manning, N. W., B. C. V. Campbell, T. J. Oxley, and R. Chapot. 2014. Acute ischemic stroke: time, penumbra, and reperfusion. Stroke 45:640–644.
2. Reinhard, M., S. Rutsch, J. Lambeck, C. Wihler, M. Czosnyka, C. Weiller, et al. 2012. Dynamic cerebral autoregulation associates with infarct size and outcome after ischemic stroke. Acta Neurol. Scand. 125:156–162.

3. Krainik, A., M. Villien, I. Troprès, A. Attyé, L. Lamalle, J. Bouvier, et al. 2013. Functional imaging of cerebral perfusion. Diagn. Interv. Imaging. Elsevier Masson SAS 94:1259–1278.

4. Deegan, B. M., E. R. Devine, M. C. Geraghty, E. Jones, G. Ólaighin, and J. M. Serrador. 2010. The relationship between cardiac output and dynamic cerebral autoregulation in humans. J. Appl. Physiol. 109:1424–1431.

5. Marik, P. E., X. Monnet, and J.-L. Teboul. 2011. Hemodynamic parameters to guide fluid therapy. Ann. Intensive Care. 21;1:1.

6. Ogoh, S., R. M. Brothers, Q. Barnes, W. L. Eubank, M. N. Hawkins, S. Purkayastha, et al. 2005. The effect of changes in cardiac output on middle cerebral artery mean blood velocity at rest and during exercise. J. Physiol. 569(Pt 2):697–704.

7. Leonardi-Bee, J., P. M. W. Bath, S. J. Phillips, and P. A. G. Sandercock. 2002. Blood pressure and clinical outcomes in the International Stroke Trial. Stroke 33:1315–1320.

8. Davis, M., B. Menon, L. Baghirzada, C. Campos-Herrera, M. Goyal, M. Hill, et al. 2012. Anesthetic management and outcome in patients during endovascular therapy for acute stroke. Anesthesiology 2:369–405.

9. Mundiyanapurath, S., A. Stehr, M. Wolf, M. Kieser, M. Mohlenbruch, M. Bendszus, et al. 2015. Pulmonary and circulatory parameter guided anesthesia in patients with ischemic stroke undergoing endovascular recanalization. J. Neurointerv. Surg. 00:1–7.

10. Okin, P. M., S. E. Kjeldsen, and R. B. Devereux. 2015. Systolic blood pressure control and mortality after stroke in hypertensive patients. Stroke 46:2113–2118.

11. Bouma, G. J., and J. P. Muizelaar. 1990. Relationship between cardiac output and cerebral blood flow in patients with intact and with impaired autoregulation. J. Neurosurg. 73:368–374.

12. Goepfert, M., H. Richter, C. Zu Eulenburg, J. Gruetzmacher, E. Rafflenbeul, K. Roeher, et al. 2013. Individually optimized hemodynamic therapy reduces complications and length of stay in the intensive care unit: a prospective, randomized controlled trial. Anesthesiology 119:824–836.

13. Kim, D. H., M. Joseph, S. Ziadi, J. Nates, M. Dannenbaum, and M. Malkoff. 2003. Increases in cardiac output can reverse flow deficits from vasospasm independent of blood pressure: a study using xenon computed tomographic measurement of cerebral blood flow. Neurosurgery 53:1044–1052.

14. Levy, M. L., C. H. Rabb, V. Zelman, and S. L. Giannotta. 1993. Cardiac performance enhancement from dobutamine in patients refractory to hypervolemic therapy for cerebral vasospasm. J. Neurosurg. 79:494–499.

15. Duke, B. J., R. E. Breeze, D. Rubenstein, B. I. Tranmer, and G. W. Kindt. 1998. Induced hypervolemia and inotropic support for acute cerebral arterial insufficiency: An underused therapy. Surg. Neurol. 49:51–57.

16. Hammer, M., T. Jovin, J. A. Wahr, and W.-D. Heiss. 2009. Partial occlusion of the descending aorta increases cerebral blood flow in a nonstroke porcine model. Cerebrovasc. Dis. 28:406–410.

17. Palumbo, D., G. Servillo, L. D'Amato, M. L. Volpe, G. Capogrosso, E. De Roberts, et al. 2006. The effects of hydroxyethyl starch solution in critically ill patients. Minerva Anestesiol. 72:655–664.

18. Keller, T. S., J. E. McGillicuddy, and V. A. K. G. LaBond. 1985. Modification of focal cerebral ischemia by cardiac output augmentation. J. Surg. Res. 39:420–432.

19. Temes, R. E., E. Tessitore, J. M. Schmidt, A. M. Naidech, A. Fernandez, N. D. Ostapkovich, et al. 2010. Left ventricular dysfunction and cerebral infarction from vasospasm after subarachnoid hemorrhage. Neurocrit. Care 13:359–365.

20. Yoneda, H., T. Nakamura, S. Shirao, N. Tanaka, H. Ishihara, E. Suehiro, et al. 2013. SMSPSG. Multicenter prospective cohort study on volume management after subarachnoid hemorrhage: hemodynamic changes according to severity of subarachnoid hemorrhage and cerebral vasospasm. Stroke 44:2155–2161.

21. Mutoh, T., K. Kazumata, S. Terasaka, Y. Taki, and A. I. T. Suzuki. 2014. Early intensive versus minimally invasive approach to postoperative hemodynamic management after subarachnoid hemorrhage. Stroke 45:1280–1284.