C. Pfluecke, M. Christoph, S. Kolschmann, D. Tarnowski, M. Forkmann, S. Jellinghaus, D. M. Poitz, C. Wunderlich, R. H. Strasser, S. Schoen, K. Ibrahim

Intra-aortic balloon pump (IABP) counterpulsation improves cerebral perfusion in patients with decreased left ventricular function

Erstveröffentlichung in / First published in:

Perfusion. 2014, 29(6), S. 511 – 516 *[Zugriff am: 19.08.2019]*. SAGE journals. ISSN 1477-111X.

DOI: https://doi.org/10.1177/0267659114525218

Original Paper

Perfusion

Perfusion
2014, Vol. 29(6) 511–516

DOI: 10.1177/0267659114525218
prf.sagepub.com
SAGE

Intra-aortic balloon pump (IABP) counterpulsation improves cerebral perfusion in patients with decreased left ventricular function

C Pfluecke,* M Christoph,* S Kolschmann, D Tarnowski, M Forkmann, S Jellinghaus, DM Poitz, C Wunderlich, RH Strasser, S Schoen and K Ibrahim

Abstract

Background: The current goal of treatment after acute ischemic stroke is the increase of cerebral blood flow (CBF) in ischemic brain tissue. Intra-aortic balloon pump (IABP) counterpulsation in the setting of cardiogenic shock is able to reduce left ventricular afterload and increase coronary blood flow. The effects of an IABP on CBF have not been sufficiently examined. We hypothesize that the use of an IABP especially enhances cerebral blood flow in patients with pre-existing heart failure.

Methods: In this pilot study, 36 subjects were examined to investigate the effect of an IABP on middle cerebral artery (MCA) transcranial Doppler (TCD) flow velocity change and relative CBF augmentation by determining velocity time integral changes (ΔVTI) in a constant caliber of the MCA compared to a baseline measurement without an IABP. Subjects were divided into two groups according to their left ventricular ejection fraction (LVEF): Group 1 LVEF >30% and Group 2 LVEF ≤30%.

Results: Both groups showed an increase in CBF using an IABP. Patients with a LVEF ≤30% showed a significantly higher increase of ΔVTI in the MCA under IABP augmentation compared to patients with a LVEF >30% (20.9% ± 3.9% Group 2 vs.10.5% ± 2.2% Group 1, p<0,05). The mean arterial pressure (MAP) increased only marginally in both groups under IABP augmentation.

Conclusions: IABP improves cerebral blood flow, particularly in patients with pre-existing heart failure and highly impaired LVEF. Hence, an IABP might be a treatment option to improve cerebral perfusion in selected patients with cerebral misperfusion and simultaneously existing severe heart failure.

Keywords

cerebral blood flow; cardiogenic shock; IABP; heart failure; cerebral perfusion; intra-aortic balloon counterpulsation

Introduction

Stroke represents a rapid loss of brain function, which most commonly results from an occlusion of a major artery in the brain. This typically leads to the death of all cells within the affected tissue and, in sequence, leads to neurological dysfunction.[1] After ischemic stroke immediate onset, it is important to provide adequate treatment with systemic thrombolysis or intra-arterial rescue procedures in order to restore cerebral blood flow.[2,3] Unfortunately, the majority of stroke patients remain ineligible for these therapies because of late hospital arrival. The ischemic cerebral infarction may be surrounded by collaterally perfused areas, the penumbra, in which vessels show an impaired autoregulation.[3] The current goal of treatment is to increase cerebral blood flow in the ischemic penumbra, which might not be

University of Technology Dresden, Heart Center Dresden, University Hospital, Dresden, Germany
*Pfluecke C. and Christoph M. contributed equally to this work

Corresponding author:
Dr. med. Christian Pfluecke
University of Technology Dresden
Heart Center Dresden
Fetscherstrasse 76
Dresden, 01307
Germany.
Email: christian.pfluecke@mailbox.tu-dresden.de

irreversibly damaged, but shows impaired perfusion. Many efforts have been made to improve cerebral perfusion as there might be salvageable brain tissue up to 8 to 24 hours after the symptoms occurred. Neither hemodilution nor treatment with vasodilators, such as pentoxifylline, have been shown to improve outcome after stroke and, therefore, are not recommended for the treatment of patients with acute ischemic stroke.[4] Inducing hypertension to increase cerebral blood flow is suggested to improve neurologic outcome.[5] Patients with acute ischemic stroke treated with intravenous phenylephrine showed an improvement in neurological symptoms in 33% of the population.[6] Unfortunately, patients with decreased left ventricular function and congestive heart failure were excluded in this setting.

The occurrence of acute ischemic stroke and coexisting heart failure is difficult to treat. Patients with a history of myocardial infarction, decreased left ventricular function[7] and consecutive left ventricular or left atrial thrombus are at a greater risk for stroke.[8,9] Due to lower cardiac output (CO), perfusion of the ischemic cerebral areas might be further reduced, which has been proven by animal and human studies.[10] Administration of vasopressors alone could have serious side effects, worsening pre-existing heart failure. How can we optimize the cerebral blood flow in patients with severely impaired left ventricular function?

Patients with cardiogenic shock (CS) are unable to maintain adequate CO. An increase in systemic vascular resistance (SVR) is typical and can worsen the heart failure by increasing the ventricular afterload.

IABP counterpulsation is the most commonly used mechanical support for the treatment of CS in selected patients.[11,12] The IABP, which is placed in the descending aorta via femoral arterial access, enhances diastolic pressure in the aortic arch by inflation of the balloon in diastole and reduces left ventricular afterload by active deflation in systole. The use of an IABP has shown a temporal improvement in CO and lower SVR.[13] Furthermore, positive effects on microvascular perfusion[14] and renal blood flow[14,15] could be demonstrated in patients with CS who were on IABP. Several studies have demonstrated the importance of establishing and maintaining a patent infarct-related artery in the setting of acute myocardial infarction complicated by cardiogenic shock.[16] The implantation of an intra-aortic balloon pump (IABP) has been shown to be able to enhance the success of coronary thrombolysis in the setting of acute myocardial infarction,[17] but did not significantly reduce 30-day mortality in patients with signs of CS after acute myocardial infarction with an early revascularization strategy. The patients in this study by Thiele et al.[18] had an average LVEF of 35%. In another randomized trial, the elective use of an IABP during high-risk percutaneous coronary interventions led to a 34% relative reduction in all-cause, long-term mortality in patients with severe ischemic cardiomyopathy. These patients had a more impaired left ventricular function (LVEF on average 23.6%).[19] Hence, the use of an IABP might prevent re-occlusion by augmenting coronary perfusion in combination with thrombolytic therapy,[20] whereas it failed to show any benefit in patients with only moderate impaired LVEF who are treated with primary angioplasty.[21]

Taking the similarity of both cerebral and myocardial ischemia into consideration, the implantation of an IABP after acute ischemic stroke and thrombolytic therapy might be feasible for improving outcome in these patients by increasing patency rates of the infarct-related artery. Furthermore, the use of an IABP could enhance cerebral blood flow, especially in the penumbra, and may provide a new treatment option in patients with acute ischemic stroke and simultaneously existing heart failure. However, it is not clear which patients might profit from the IABP by augmenting cerebral perfusion.

The aim of this pilot study was to examine the hemodynamic effects of an IABP on cerebral blood flow in patients with severely impaired left ventricular function.

Methods

Thirty-six subjects were examined to determine the effect of the IABP on middle cerebral artery (MCA) transcranial Doppler (TCD) flow velocity change and cerebral flow augmentation compared to a baseline measurement without an IABP. All the patients were undergoing coronary angiography, either due to acute coronary syndrome or elective high-risk percutaneous coronary intervention (PCI). The IABP was inserted in the cardiac catheterization laboratory via the femoral artery using an 8.0 Fr intra-aortic balloon catheter (Fidelity IAB Catheter, Maquet Cardiopulmonary AG, Hirrlingen, Germany). Afterwards, the patients were transferred to the intensive care unit. The balloon size was adapted to the subject's height. IABP inflation and deflation timing was optimized automatically by the IABP. The position of the IABP was controlled by chest X-ray.

Measurements of transcranial blood flow velocities were performed as previously described.[22] To determine the effect of the IABP on MCA cerebral flow, subjects were on 1:1 augmentation by IABP for at least one hour before the measurements of MCA TCD flow velocity change and velocity time integral (Figure 1) were performed (Phillips HD 11, S3-1, 3 to 1 MHz, Philips GmbH, Herrsching, Germany).

Afterwards, the IABP was paused for 1 minute and changes in the parameters mentioned above were

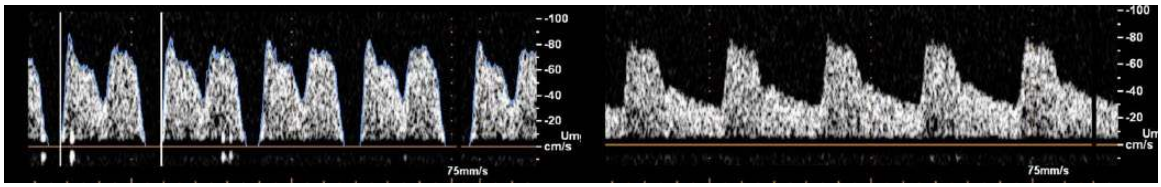

Figure 1. Measurement of transcranial Doppler (TCD) flow velocity of the middle cerebral artery (MCA) with and without the intra-aortic balloon pump (IABP).
The picture shows a representative example of transcranial Doppler (TCD) flow measurement of the middle cerebral artery (MCA).
left: typical bimodal curve shows the increased mean cerebral blood velocity due to the increased diastolic cerebral blood flow while the IABP is operating.
right: normal cerebral blood flow pattern in the MCA while the IABP is turned off.

Table 1. Baseline characteristics.

Table 1	Overall	LVEF>30% (Group 1) n=26	LVEF≤30% (Group 2) n=10	p-value
Age (years)	69.1 ± 10.1	68.3 ± 2.1	71.2 ±2.5	0.46
Female n (%)	10 (27.8)	7 (27)	3 (30)	0.86
Death n (%)	5 (13.9)	2 (7.7)	3 (30)	0.19
LVEF (%)	39.7 ± 11.2	44.3 ± 9.6	27.7 ± 3.4	<0.01
MAP with IABP in mmHg	81.5 ± 3.9	80.7 ± 3.7	81.8 ± 3.9	0.87
MAP without IAPB in mmHg	75.9 ± 2.3	76.0 ± 2.0	75.9 ± 2.5	0.62
Aspirin n (%)	36 (100)	26 (100)	10 (100)	
Clopidogrel n (%)	35 (97.2)	26 (100)	9 (90)	0.95
Heparin (%)	36 (100)	26 (100)	10 (100)	
HR with IABP (beats/min)	82.7 ± 16.4	80.9 ± 13.5	91.4 ± 16.9	0.44
HR without IABP (beats/min)	82.1 ± 16.0	80.4 ± 12.6	90.4 ± 17.8	0.47
TAPSE (mm)	22.1 ± 5.3	22.4 ± 1.2	20.8 ± 2.3	0.55
RVESP (mmHg)	36.9 ± 12.2	35.6 ± 2.6	40.3 ± 4.3	0.36
Dobutamine n (%)	39.2 ± 4.9	35.0 ± 4.8	50.0 ± 5.2	0.41
Noradrenaline n (%)	33.4 ± 4.7	27.0 ± 4.5	50.0 ± 5.2	0.19

Values represent numbers of patients (n) with percentages in parenthesis or mean ± standard error, as appropriate. LVEF: left ventricular ejection fraction; MAP: mean arterial pressure; IABP: intra-aortic balloon pump; HR: heart rate; TAPSE: tricuspid annular plane systolic excursion; RVESP: right ventricular systolic pressure.

measured. The cerebral blood flow (CBF) in the MCA could be calculated as:

$$CBF = VTI * HR * \pi VD / 4$$

VTI: velocity time integral; HR: heart rate; VD: vessel diameter.

Measurements were taken in the same section of the MCA to ensure a constant vessel diameter. Differences in heart rate in the measurements with and without IABP were negligible (Table 1). Therefore, the relative change in cerebral blood flow corresponds to the relative change of VTI.

$$\Delta CBF \sim \Delta VTI$$

The subjects were divided into two groups according to their ejection fraction (Group 1: LVEF >30%, Group 2: LVEF ≤30%). The chosen cut-off point for the left ventricular ejection fraction (LVEF) of 30% reflects the transition to severe impairment of systolic left heart function. LVEF was measured by echocardiography following the Simpson method.

Statistical analyses were performed by a statistician using SPSS v.19 (IBM SPSS Inc., Austin, TX). The distribution of continuous data was examined using the Kolmogorow-Smirnov test. Data with a normal Gaussian distribution were analyzed using Student´s t-test, data with a non-Gaussian distribution were analyzed using the Mann-Whitney U test. Categorical data were compared using the Chi-square test, except when the absolute number of events in each group was <5, in which case Fisher's exact test was used. P-values ≤0.05 were considered as statistically significant.

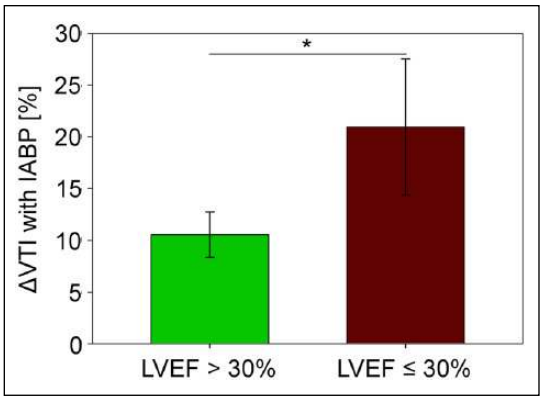

Figure 2. Improved cerebral blood flow in patients with LVEF≤30% using an IABP.
The chart shows the improvement of velocity time integral (ΔVTI), which corresponds in this setting (ΔCBF~VTI) to the improvement of cerebral blood flow in patients with an IABP according to their left ventricular function, LVEF >30% vs. LVEF ≤30%.
* $p<0.05$. Chart shows mean ± standard error.

Results

Baseline characteristics of all 36 patients are shown in Table 1. The mean LVEF in Group 1 was 44.3% ± 9.6%, compared to Group 2 with a LVEF of 27.7% ± 3.4%. The implantation of an IABP was able to improve the mean cerebral blood flow in patients with a highly impaired left ventricular function as well as in patients with normal or slightly impaired LVEF. However, patients with a LVEF ≤30% had a significantly higher augmentation of cerebral blood flow with the IABP compared to patients with a LVEF>30%. The improvement of the cerebral blood flow, measured in MCA TDC flow velocity change, reached 20.9% (± 3.9%) in Group 2 vs. 10.5% (± 2.2%) in Group 1 ($p<0.05$) (Figure 2). No severe complications (major bleeding or stroke) due to the implantation of an IABP were registered. Only two minor bleeds occurred in Group 1. The usage of sympathomimetic drugs was slightly higher in patients with highly impaired left ventricular function (Group 2), but did not reach significant values. The mean arterial pressure (MAP) before implantation of an IABP was similar in both groups. The MAP was increased only marginally after IABP implantation in both groups, without any significance.

Discussion

In the present study, we showed that an IABP augments cerebral blood flow. The increase of cerebral blood flow was significantly higher with 20% augmentation in subjects with severe heart failure compared to patients with slightly reduced left ventricular function. The higher augmentation of cerebral blood flow in subjects with highly decreased left ventricular function might be due to the direct effect of the IABP, with displacement of blood volume and, consequently, the improvement of CO with the increase in coronary blood flow. Since right heart catheters were not routinely used during the procedures, we could only speculate that the compensatory increased in SVR might be reduced by the use of an IABP as it was previously reported.[13] As the CBF was increased in a constant caliber of the main vessel, we assume that the patients on an IAPB had an increased CO. Since the decrease in mean arterial pressure in patients with an IABP was absent, we postulate a decrease in SVR (MAP = CO x SVR) as a possible explanation for the presumably increased CO.

Both the decrease in left ventricular afterload and the increase in cerebral perfusion could be beneficial to patients with acute ischemic stroke and simultaneously existing severe heart failure. These data reflect other studies that proved an increased cerebral flow using external counterpulsation in a small cohort of subjects.[21,23] In subjects with vasospasm, the increase in cerebral blood flow was achieved using a partial aortic obstruction by an intra-aortic inflation device which diverts blood flow from the systemic circulation toward the cerebral circulation.[24] Contrary to the partial aortic obstruction, the IABP achieved an increase in mean CBF by augmenting, predominantly, the diastolic CBF. Normally, cerebral blood flow (CBF) is kept constant within a wide range (60 to 150 mmHg) of mean arterial pressures (MAP) whereas the CBF in patients with chronic heart failure can be reduced substantially. Experimental data suggested that the cerebral arteriolar dilatory capacity becomes nearly exhausted in patients with severe heart failure.[24,25] It is probable that enhancement of cardiac output rather than raised arterial blood pressure is able to increase CBF in patients with low cardiac output. It has been demonstrated that reduced CBF in patients with severe heart failure could be normalized after successful heart transplantation.[10] Therefore, the use of an IABP is safe even after the use of fibrinolytics and combined platelet aggregation inhibitors. The implantation of an IABP can be performed at the bedside and requires minimum expertise. The concomitant treatment of stroke and heart failure will be of vital relevance in future. In these patients, the temporary use of an IABP could provide a special benefit by improving the cerebral blood flow. Limitations of this pilot study are: a relatively small number of subjects treated with an IABP, all the patients had cardiac diseases, but no strokes were investigated. Furthermore, no long-term outcome was noted. However, the use of an IABP seemed to be able to enhance cerebral blood flow, especially in patients with severe impaired heart function. The increase in mean CBF is presumably due to an augmented diastolic CBF. The clinical relevance of an isolated augmentation of diastolic CBF currently cannot be

assessed.[26,27] The common use of heparin anticoagulation in patients receiving an IABP could be difficult in patients with acute ischemic stroke.[28] However, no convincing data for the necessity of anticoagulation in patients with IABP currently exists.[29,30] The literature suggests that it is safe to omit heparinization when using IABP counterpulsation.[31] Considering the fact that current therapy options for increasing CBF barely exist, the temporary use of an IABP could provide a new treatment option in selected patients with acute ischemic stroke and simultaneous severe heart failure, especially if there is a need to use a high dose of sympathomimetic drugs for maintaining an adequate blood pressure. Further studies have to address the question if the implantation of an IABP in subjects with acute stroke and severe heart failure could achieve a neurological improvement.

Declaration of conflicting interest

The authors have no conflicts of interest to declare.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

References

1. Sims NR, Muyderman H. Mitochondria, oxidative metabolism and cell death in stroke. *Biochim Biophys Acta* 2010; 1802: 80–91.
2. Kern R, Nagayama M, Toyoda K, Steiner T, Hennerici MG, Shinohara Y. Comparison of the European and Japanese guidelines for the management of ischemic stroke. *Cerebrovasc Dis* 2013; 35: 402–418.
3. Saeed NP, Panerai RB, Horsfield MA, Robinson TG. Does stroke subtype and measurement technique influence estimation of cerebral autoregulation in acute ischaemic stroke? *Cerebrovasc Dis* 2013; 35: 257–261.
4. Adams HP Jr., del Zoppo G, Alberts MJ, et al. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/ American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups. The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. *Circulation* 2007 22; 115: e478–e534.
5. Rordorf G, Cramer SC, Efird JT, Schwamm LH, Buonanno F, Koroshetz WJ. Pharmacological elevation of blood pressure in acute stroke. Clinical effects and safety. *Stroke* 1997; 28: 2133–2138.
6. Rordorf G, Koroshetz WJ, Ezzeddine MA, Segal AZ, Buonanno FS. A pilot study of drug-induced hypertension for treatment of acute stroke. *Neurology* 2001; 56: 1210–1213.
7. Pullicino PM, Thompson JL, Sacco RL, et al. Stroke in heart failure in sinus rhythm: the warfarin versus aspirin in reduced cardiac ejection fraction trial. *Cerebrovasc Dis* 2013; 36: 74–78.
8. Corley SD, Epstein AE, DiMarco JP, et al. Relationships between sinus rhythm, treatment, and survival in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Study. *Circulation* 2004; 109: 1509–1513.
9. Freeman WD and Aguilar MI. Prevention of cardioembolic stroke. *Neurotherapeutics* 2011; 8: 488–502.
10. Gruhn N, Larsen FS, Boesga-ard S, et al. Cerebral blood flow in patients with chronic heart failure before and after heart transplantation. *Stroke* 2001; 32: 2530–2533.
11. Moulopoulos S, Stamatelopoulos S, Petrou P. Intra-aortic balloon assistance in intractable cardiogenic shock. *Eur Heart J* 1986; 7: 396–403.
12. Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2012; 33: 2569–2619.
13. Prondzinsky R, Lemm H, Swyter M, et al. Intra-aortic balloon counterpulsation in patients with acute myocardial infarction complicated by cardiogenic shock: the prospective, randomized IABP SHOCK Trial for attenuation of multiorgan dysfunction syndrome. *Crit Care Med* 2010; 38: 152–160.
14. Jung C, Lauten A, Rodiger C, Krizanic F, Figulla HR, Ferrari M. Effect of intra-aortic balloon pump support on microcirculation during high-risk percutaneous intervention. *Perfusion* 2009; 24: 417–421.
15. Sloth E, Sprogoe P, Lindskov C, Horlyck A, Solvig J, Jakobsen C. Intra-aortic balloon pumping increases renal blood flow in patients with low left ventricular ejection fraction. *Perfusion* 2008; 23: 223–226.
16. Kammler J, Kypta A, Hofmann R, et al. TIMI 3 flow after primary angioplasty is an important predictor for outcome in patients with acute myocardial infarction. *Clin Res Cardiol* 2009; 98: 165–170.
17. Sanborn TA, Sleeper LA, Bates ER, et al. Impact of thrombolysis, intra-aortic balloon pump counterpulsation, and their combination in cardiogenic shock complicating acute myocardial infarction: a report from the SHOCK Trial Registry. SHould we emergently revascularize Occluded Coronaries for cardiogenic shocK? *J Am Coll Cardiol* 2000; 36: 1123–1129.
18. Thiele H, Zeymer U, Neumann FJ, et al. Intra-aortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med* 2012; 367: 1287–1296.
19. Perera D, Stables R, Clayton T, et al. Long-term mortality data from the balloon pump-assisted coronary intervention study (BCIS-1): a randomized, controlled trial of elective balloon counterpulsation during high-risk percutaneous coronary intervention. *Circulation* 2013; 127: 207–212.
20. Barron HV, Every NR, Parsons LS, et al. The use of intra-aortic balloon counterpulsation in patients with cardiogenic shock complicating acute myocardial infarction: data from the National Registry of Myocardial Infarction 2. *Am Heart J* 2001; 141: 933–939.

21. Patel MR, Smalling RW, Thiele H, et al. Intra-aortic balloon counterpulsation and infarct size in patients with acute anterior myocardial infarction without shock: the CRISP AMI randomized trial. *JAMA* 2011; 306: 1329–1337.
22. Purkayastha S, Sorond F. Transcranial Doppler ultrasound: technique and application. *Semin Neurol* 2012; 32: 411–420.
23. Alexandrov AW, Ribo M, Wong KS, et al. Perfusion augmentation in acute stroke using mechanical counter-pulsation-phase IIa: effect of external counterpulsation on middle cerebral artery mean flow velocity in five healthy subjects. *Stroke* 2008; 39: 2760–2764.
24. Lylyk P, Vila JF, Miranda C, Ferrario A, Romero R, Cohen JE. Partial aortic obstruction improves cerebral perfusion and clinical symptoms in patients with symptomatic vasospasm. Neurol Res 2005; 27: S129-S135.
25. Georgiadis D, Sievert M, Cencetti S, et al. Cerebrovascular reactivity is impaired in patients with cardiac failure. *Eur Heart J* 2000; 21: 407–413.
26. Hansen JH, Schlangen J, Voges I, et al. Impact of afterload reduction strategies on regional tissue oxygenation after the Norwood procedure for hypoplastic left heart syndrome. *Eur J Cardiothorac Surg* 2014; 45: e13–19.
27. Varsos GV, Richards HK, Kasprowicz M, et al. Cessation of diastolic cerebral blood flow velocity: the role of critical closing pressure. *Neurocrit Care* 2014; 20: 40–48.
28. Matute MC, Masjuan J, Egido JA, et al. Safety and outcomes following thrombolytic treatment in stroke patients who had received prior treatment with anticoagulants. *Cerebrovasc Dis* 2012; 33: 231–239.
29. Jiang CY, Zhao LL, Wang JA, Mohammod B. Anticoagulation therapy in intra-aortic balloon counterpulsation: does IABP really need anti-coagulation? *J Zhejiang Univ Sci* 2003; 4: 607–611.
30. Cooper HA, Thompson E, Panza JA. The role of heparin anticoagulation during intra-aortic balloon counterpulsation in the coronary care unit. *Acute Card Care* 2008; 10 :214–220.
31. Pucher PH, Cummings IG, Shipolini AR, McCormack DJ. Is heparin needed for patients with an intra-aortic balloon pump? *Interact Cardiovasc Thorac Surg* 2012; 15: 136–139.