Accepted August 2014

REVIEW

# The intra-aortic balloon pump keeps pumping, but in selected patients

**C.A. den Uil, J.M. Cheng, L.S.D. Jewbali, K. Nieman, K.M. Akkerhuis, E.A. Dubois, F. Zijlstra**

Thoraxcenter, Erasmus Medical Center, Departments of Cardiology and Intensive Care Medicine, Rotterdam, the Netherlands

Correspondence

C.A. den Uil – email: c.denuil@erasmusmc.nl

Key words – **Acute myocardial infarction, cardiogenic shock, clinical trials, intra-aortic balloon pump, mechanical circulatory support, percutaneous coronary intervention**

## Abstract

In recent years, three randomised controlled trials questioned the use of the intra-aortic balloon pump (IABP) in populations of high-risk PCI (BCIS-1), acute myocardial infarction (CRISP-AMI), and cardiogenic shock (IABP-SHOCK II). This review describes these and other IABP trials, as well as their outcome on mortality. Clinical implications are addressed. There is a pressing need for adequately powered randomised controlled trials testing the optimal timing of mechanical circulatory support as well as device design in cardiogenic shock.

## Introduction

Dr. Adrian Kantrowitz introduced the intra-aortic balloon pump (IABP) in the 1960s (*figure 1*). He used large balloon catheters inserted in the aorta by surgical cut down of the femoral artery. From the late 1970s placement of the balloon was modified using the Seldinger technique. Until recently, the intra-aortic balloon pump was increasingly being used to support haemodynamics in patients with acute myocardial infarction complicated by cardiogenic shock, ventricular septal rupture or acute mitral regurgitation,[1,2] as well as in patients undergoing high-risk percutaneous coronary intervention (PCI), prior to high-risk cardiac surgery,[3,4] in postcardiotomy cardiogenic shock, refractory heart failure,[5] and with refractory ventricular arrhythmias[6]. Its physiological effects in reducing afterload and improving coronary perfusion were believed to enhance survival in these groups of patients, especially because complication rates (access site bleeding and vascular complications) were low.[1,7] However, evidence supporting the use of IABP in these clinical settings was mainly based on registry data.[8] In recent years, three randomised controlled trials questioned the use of IABP in subsequently high-risk PCI, acute myocardial infarction, and cardiogenic shock. The aim of this review is to discuss these trials and to evaluate the current role of intra-aortic balloon pump counterpulsation in high-risk PCI and acute myocardial infarction with or without shock.

## Haemodynamics

The intended haemodynamic relief from the IABP is twofold. During diastole, the IABP inflates thereby displacing blood from the descending aorta. It then deflates immediately before systole creating a void in the aorta.[9] These mechanisms produce the haemodynamic effects of increasing diastolic, mean arterial and coronary perfusion pressures, while decreasing afterload. In serial measurements, IABP counterpulsation acutely lowers left ventricular end-diastolic pressure and modestly increases the cardiac index and cardiac power index.[10] Sustained haemodynamic benefit was contradicted by the results of a recent small randomised trial.[11] These investigators demonstrated that, in patients with complicated myocardial

**Figure 1.** Development in balloon pump consoles. Panel A: One of the first IABP consoles. Panel B: Modern miniaturised portable console


Courtesy of MACQUET Cardiovascular, Datascope Corp., Mahwah, NJ, USA.

infarction, haemodynamic improvement in the days following IABP implantation did not significantly differ from the control group. However, this study was clearly underpowered and baseline haemodynamic parameters significantly differed between the two treatment arms.[11]

## High-risk percutaneous coronary intervention

The Balloon-Pump Assisted Coronary Intervention Study (BCIS-1) investigated balloon pump support in 301 elective patients undergoing high-risk PCI: left ventricular ejection fraction (LVEF) ≤ 30% and unprotected left main coronary artery or target vessel supply ≥40% of myocardium (*table 1*).[12] Prolonged procedural hypotension occurred more frequently in the group with no planned IABP insertion. Moreover, rescue IABP insertion was required in 18 patients (12%) assigned to have no planned IABP insertion. There was no difference in major adverse cardiac events and all-cause mortality at six-month follow-up. At long-term follow-up, elective IABP support during PCI was associated with a 34% relative reduction in all-cause mortality compared with unsupported PCI (p = 0.04, absolute difference 11%).[13]

## Acute myocardial infarction

Several randomised trials investigated the use of IABP support in patients with large, mainly anterior wall, myocardial infarction without evidence of cardiogenic shock (*table 2*). Most studies demonstrated that systematic use of intra-aortic balloon pumping after primary angioplasty or coronary stenting did not lead to myocardial salvage, nor to a better clinical outcome in terms of major adverse cardiac events or all-cause mortality. However, most studies were underpowered to detect a difference in mortality. Counterpulsation Reduces Infarct Size pre-PCI (CRISP) was a large randomised trial (337 patients) that evaluated the role of IABP support started prior to PCI in anterior STEMI without cardiogenic shock.[14] No difference was observed in the primary endpoint (infarct size assessed by cardiac magnetic resonance imaging) in the IABP group, compared with the control group. All-cause mortality at six months was less frequent in the IABP group, but the number of events was low and not significantly different (1.9 vs. 5.2%, *table 2*). Preliminary observational data suggest that IABP insertion before primary PCI might in fact result in larger infarct sizes,[7] presumably due to the (short) delay in

**Table 1.** Characteristics and outcome of randomised controlled clinical trials on intra-aortic balloon pump support compared with conventional therapy in high-risk elective PCI

| Trial (year) | Population | Intervention (I/C) | Sample size | Intervention not performed in I | Intervention performed in C | Median duration of support | Longest reported time point | Number of deaths (I/C) | OR or HR for mortality |
|---|---|---|---|---|---|---|---|---|---|
| BCIS-1 (2010)[12] | High-risk PCI | PCI+IABP/ PCI | 151/150 | 3(2%) | 18(12%) | < 24 h | 6-month | 7/151 11/150 | 0.61 [0.24-1.62] |
| BCIS-1 (2013)[13] | High-risk PCI | PCI+IABP/ PCI | 151/150 | 3(2%) | 18(12%) | < 24 h | 51-month | 42/151 58/150 | 0.66 [0.44-0.98] |

I = intervention (IABP), C = control (medical management)
PCI = percutaneous coronary intervention; IABP = intra-aortic balloon pump; OR = odds ratio; HR = hazard ratio (risk ratio not significantly different from 1 indicated in orange, otherwise in blue)

**Table 2.** Characteristics and outcome of randomised controlled clinical trials on intra-aortic balloon pump support compared with conventional therapy in acute myocardial infarction without shock

| Trial (year) | Population | Intervention (I/C) | Sample size | Intervention not performed in I | Intervention performed in C | Median duration of support | Longest reported time point | Number of deaths (I/C) | OR or HR for mortality |
|---|---|---|---|---|---|---|---|---|---|
| Ohman (1994)[26] | Primary PTCA | PTCA+IABP/ PTCA | 96/86 | 0(0%) | 7(8%) | 48 h | In-hospital | 2/96 2/86 | 0.90 [0.13-6.22] |
| PAMI-II (1997)[27] | Primary PTCA | PTCA+IABP/ PTCA | 211/226 | 29(14%) | 26(12%) | 36-48 h | In-hospital | 9/211 7/226 | 1.38 [0.52-3.63] |
| Van 't Hof (1999)[28] | Primary or rescue PTCA | PTCA+IABP/ PTCA | 118/120 | 30(25%) | 37(31%) | 48 h | 6-month | 12/118 9/120 | 1.36 [0.59-3.10] |
| Vijayalakshmi (2007)[29] | High-risk PCI | PCI+IABP/ PCI | 17/16 | Not reported | Not reported | 48 h | In-hospital | 3/17 0/16 | 6.61 [0.37-118.7] |
| CRISP AMI (2011)[14] | Primary PCI | PCI+IABP/ PCI | 161/176 | 8(5%) | 15(9%) | < 24 h | 6-month | 3/161 9/176 | 0.36 0.10-1.32] |
| Gu (2011)[30] | Primary PCI | PCI+IABP/ PCI | 51/55 | Not reported | Not reported | 48 h | 6-month | 9/51 18/55 | 0.54 [0.27-1.09] |

I = intervention (IABP), C = control (medical management)
PTCA = percutaneous transluminal coronary angioplasty; PCI = percutaneous coronary intervention; IABP = intra-aortic balloon pump; OR = odds ratio; HR = hazard ratio (risk ratios not significantly different from 1 are indicated in orange)

coronary revascularisation (myocardial reperfusion) associated with upstream implantation of the pump.

## Acute myocardial infarction complicated by cardiogenic shock

The IABP-SHOCK II trial randomised 600 patients with acute myocardial infarction complicated by cardiogenic shock to IABP support or not.[15] Ninety-six percent of the patients received primary PCI. The primary endpoint of 30-day all-cause mortality was not different between the two treatment arms (40% in the IABP group vs. 41% in controls, p = 0.69, *table 3*).

The sample size calculation for the IABP SHOCK II trial was based on an anticipated 30-day mortality of 56% in the control group, where the observed mortality rate was about 40%. Therefore, despite having randomised 600 patients, the trial still lacked sufficient power to address its primary hypothesis definitively.[16] In addition, several other issues thwart interpretation of the study results. First, there were no haemodynamic requirements to confirm the diagnosis of cardiogenic shock. Second, in one-fourth of the patients, the right coronary artery was the infarct-related vessel and right ventricular infarction (which is not a good indication for IABP) might have contributed to haemodynamic compromise. Third, since a study using balloon pumps (in sick patients) could not be blinded, cross-over occurred in 10% of the control arm. Fourth, ten patients assigned to the IABP group died before an IABP could be inserted, which might have influenced the results. Finally, all-cause, and not cardiovascular, mortality rates were reported. Since nearly half of the patients received cardiopulmonary resuscitation before randomisation, it is possible that a neurological cause of death (which is not positively affected by IABP) may have superseded cardiovascular death.

## IABP vs. percutaneous left ventricular assist devices

The more powerful percutaneous left ventricular assist devices (pLVADs) can directly unload the left ventricle by withdrawing blood from the left atrium after transseptal puncture (TandemHeart) or, somewhat less invasively, by aspirating blood from the left ventricle through retrograde crossing of the aortic valve (Impella).[17] pLVADS would potentially afford the left ventricle with more haemodynamic support. The PROTECT-II study randomised patients undergoing elective high-risk PCI (last patent vessel with LVEF ≤35%, unprotected left main, or three-vessel disease with LVEF ≤30%) to support with either IABP or Impella 2.5.[18] The primary endpoint (a composite of 30-day major adverse events) was not statistically different between the two groups. However, there was a trend for less major adverse events associated with Impella support at 90 days. All-cause mortality was not different at one- and three-month follow-up (*table 4*).

Three small randomised trials compared TandemHeart[19,20] or Impella[21] versus IABP support in the setting of cardiogenic shock. Use of these percutaneous LVAD systems provided superior haemodynamic support compared with the IABP; however, this did not translate into lower 30-day mortality (pooled relative risk 1.06 [0.68-1.66]).[22] Significant bleeding was observed more frequently in patients treated with a TandemHeart.

## Conclusions and current perspectives

Most of the above-mentioned IABP trials could not demonstrate a clinical benefit; however, almost all these trials, especially when mortality was used as endpoint, were underpowered. When we take this into account, which conclusions could be drawn from these trials? First, based on BCIS-1, IABP support may lower mortality in the setting of high-risk elective PCI, where the Impella device remains an alternative, more powerful, way of support, especially if a higher output can be generated such as may be accomplished with the Impella 5.0.[13,18,23] Second, CRISP-AMI demonstrated that routine implantation of an IABP in acute myocardial infarction is not useful and this result is in line with other observations.[14] Finally, the IABP-SHOCK II trial data are difficult to interpret. We may conclude that routine IABP implantation beyond

**Table 3.** Characteristics and outcome of randomised controlled clinical trials on intra-aortic balloon pump support compared with conventional therapy in acute myocardial infarction complicated by cardiogenic shock

| Trial (year) | Population | Intervention (I/C) | Sample size | Intervention not performed in I | Intervention performed in C | Median duration of support | Longest reported time point | Number of deaths (I/C) | OR or HR for mortality |
|---|---|---|---|---|---|---|---|---|---|
| TACTICS (2005)[31] | Thrombolysis or rescue PCI | TT±PCI+IABP/ TT±PCI | 30/27 | 3(10%) | 9(33%) | 48 h | 6-month | 10/30 12/27 | 0.75 [0.39-1.45] |
| IABP-SHOCK II (2012)[15] | Primary PCI | PCI+IABP/ PCI | 300/298 | 13(4%) | 30(10%) | 72 h | 30-days | 119/300 123/298 | 0.96 [0.79-1.17] |
| IABP-SHOCK II (2013)[25] | Primary PCI | PCI+IABP/ PCI | 299/296 | 13(4%) | 30(10%) | 72 h | 12-month | 155/299 152/296 | 1.01 [0.86-1.18] |

I = intervention (IABP), C = control (medical management)
PCI = percutaneous coronary intervention; IABP = intra-aortic balloon pump; OR = odds ratio; HR = hazard ratio (risk ratio's not signifantly different from 1 are indicated in orange)

**Table 4.** Characteristics and outcome of randomised controlled clinical trials on intra-aortic balloon pump compared with percutaneous left ventricular assist device (LVAD) support

| Trial (year) | Population | Intervention (I/C) | Sample size | Intervention not performed in I | Inter-vention performed in C | Median duration of support | AMI | Shock | Longest reported time point | Number of deaths (I/C) | OR or HR for mortality |
|---|---|---|---|---|---|---|---|---|---|---|---|
| PROTECT-II (2012)[18] | High-risk PCI | PCI+Impella 2.5/ PCI+IABP | 225/222 | 0 (0%) | 0 (0%) | LVAD 1.9 h/ IABP 8.4 h | No | No | 3 month | 19/222 27/225 | 0.71 [0.41-1.24] |
| Thiele (2005)[19] | Cardiogenic shock | PCI+ TandemHeart/ PCI + IABP | 21/20 | 0(0%) | 1(5%) | LVAD 96 h/ IABP84 h | Yes | Yes | 30-day | 9/20 9/21 | 0.95 [0.48-1.90] |
| Burkhoff (2006)[20] | Cardiogenic shock | TandemHeart/ IABP | 19/14 | 0(0%) | 0(0%) | LVAD 48 h/ IABP 46 h | 70% | Yes | 30-day | 9/19 5/14 | 1.33 [0.57-3.10] |
| Seyfarth (2008)[21] | Cardiogenic shock | Impella 2.5/ IABP | 13/13 | 1(8%) | 1(8%) | LVAD 25 h/ IABP 23 h | Yes | Yes | 30-day | 6/13 6/13 | 1.00 [0.44-2.29] |

I = intervention (percutaneous LVAD), C = control (IABP)
PCI = percutaneous coronary intervention; IABP = intra-aortic balloon pump; OR = odds ratio; HR = hazard ratio (risk ratios not significantly different from 1 are indicated in orange)

common intropic support in cardiogenic shock probably has no benefit.[24,25] The problem in these 'crash and burn' patients, however, is that there is no proven alternative for the balloon pump in case of inevitably necessary mechanical circulatory support. We are still awaiting the results of an adequately powered randomised trial of a percutaneous left ventricular assist device (probably Impella) in cardiogenic shock, compared with IABP. In the meantime the IABP keeps pumping, while we propose restricted use in carefully selected patients undergoing high-risk PCI or those with evidence of persistent circulatory failure despite pharmacological support.

## References


1. Cheng JM, Valk SD, den Uil CA, et al. Usefulness of intra-aortic balloon pump counterpulsation in patients with cardiogenic shock from acute myocardial infarction. Am J Cardiol. 2009;104:327-32.
2. Valk SD, Cheng JM, den Uil CA, et al. . Encouraging survival rates in patients with acute myocardial infarction treated with intra-aortic balloon pump. Neth Heart J. 2011;19:112-8.
3. Den Uil CA, Valk SD, Cheng JM, et al. Prognosis of patients undergoing cardiac surgery and treated with intra-aortic balloon pump counterpulsation prior to surgery: a long-term follow-up study. Interact Cardiovasc Thorac Surg. 2009;9:227-31.
4. Theologou T, Bashir M, Rengarajan A, Khan O, Spyt T, Richens Dea. Preoperative intra aortic balloon pumps in patients undergoing coronary artery bypass grafting. Cochrane Database Syst Rev. 2011;1:CD004472.
5. Gjesdal O, Gude E, Arora S, et al. Intra-aortic balloon counterpulsation as a bridge to heart transplantation does not impair long-term survival. Eur J Heart Fail. 2009;11:709-14.
6. Fotopoulos G, Mason M, Walker S, et al. Stabilisation of medically refractory ventricular arrhythmia by intra-aortic balloon counterpulsation. Heart. 1999;82:96-100.
7. Cheng JM, van Leeuwen MA, de Boer SP, Wai MC, den Uil CA, Jewbali LS, et al. Impact of intra-aortic balloon pump support before versus after primary percutaneous coronary intervention in patients with cardiogenic shock from acute myocardial infarction. Int J Cardiol 2013; 168(4):3758-3763.
8. Sjauw KD, Engström AE, Vis MM, van der Schaaf RJ, Baan JJ, Koch K, et al. A systematic review and meta-analysis of intra-aortic balloon pump therapy in ST-elevation myocardial infarction: should we change the guidelines? Eur Heart J 2009; 30(4):459-468.
9. Santa-Cruz RA, Cohen MG, Ohman EM. Aortic counterpulsation : a review of the hemodynamc effects and indications for use. Catheter Cardiovasc Interv 2006; 67(1):68-77.
10. Den Uil CA, Lagrand WK, van der Ent M, Jewbali LS, Brugts JJ, Spronk PE, et al. The effects of intra-aortic balloon pump support on macrocirculation and tissue microcirculation in patients with cardiogenic shock. Cardiology 2009; 114(1):42-46.
11. Prondzinsky R, Unverzagt S, Russ M, Lemm H, Swyter M, Wegener N, et al. Hemodynamic effects of intra-aortic balloon counterpulsation in patients with acute myocardial infarction complicated by cardiogenic shock: the prospective, randomized IABP shock trial. Shock 2012; 101(5):378-384.
12. Perera D, Stables R, Thomas M, Booth J, Pitt M, Blackman D, et al. Elective intra-aortic balloon counterpulsation during high-risk percutaneous coronary intervention: a randomized controlled trial. JAMA 2010; 304(8):867-874.
13. Perera D, Stables R, Clayton T, De Silva K, Lumley M, Clack Lea. Long-term mortality data from the balloon pump-assisted coronary intervention study (BCIS-1) : a randomized controlled trial of effective balloon counterpulsation during high-risk percutaneous coronary intervention. Circulation 2013; 127(2):207-212.
14. Patel MR, Smalling RW, Thiele H, Barnhart HX, Zhou Y, Chandra P, 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(12):1329-1337.
15. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, et al. Intraaortic balloon pump support for myocardial infarction with cardiogenic shock. N Engl J Med 2012; 367(14):1287-1296.
16. Perera D, Lumley M, Pijls N, Patel MR. Intra-aortic balloon pump trials: Questions, answers and unresolved issues. Circ Cardiovasc Interv 2013; 6:317-321.
17. Engström AE, de Mol BAJM, Lagrand WK, Henriques JPS. The Impella system as a "bridge to recovery": a case series of four ST-elevation myocardial infarction patients presenting with cardiogenic shock. Neth J Crit Care 2011; 15(6):280-287.
18. O'Neill WW, Kleiman NS, Moses J, Henriques JP, Dixon S, Massaro J, et al. . A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: the PROTECT II study. Circulation 2012; 126(14):1717-1727.
19. Thiele H, Sick P, Boudriot E, Diederich KW, Hambrecht R, Niebauer J, et al. . Randomized comparison of intra-aortic balloon pump support with a percutaneous left ventricular assist device in patients with revascularized acute myocardial infarction complicated by cardiogenic shock. Eur Heart J 2005; 26(13):1276-1283.
20. Burkhoff D, Cohen H, Brunckhorst C, O'Neill WW. A randomized multicenter clinical study to evaluate the safety and efficacy of the TandemHeart percutaneous ventricular assist device versus conventional therapy with intraaortic balloon pumping for treatment of cardiogenic shock. Am Heart J 2006; 152(3):e461-468.
21. Seyfarth M, Sibbing D, Bauer I, Frohlich G, Bott-Flugel L, Byrne R, et al. . A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left ventricular assist device versus intra-aortic balloon pumping for treatment of cardiogenic shock caused by myocardial infarction. J Am Coll Cardiol 2008; 52(19):1584-1588.
22. Cheng JM, den Uil CA, Hoeks SE, van der Ent M, Jewbali LS, van Domburg RT, et al. Percutaneous left ventricular assist devices vs. intra-aortic balloon pump counterpulsation for treatment of cardiogenic shock: a meta-analysis of controlled trials. Eur Heart J 2009; 30(17):2102-2108.

23. Engström AE, Cocchieri R, Driessen AH, Sjauw KD, Vis MM, Baan J, de Jong M, Lagrand WK, van der Sloot JA, Tijssen JG, de Winter RJ, de Mol BA, Piek JJ, Henriques JP. The Impella 2.5 and 5.0 devices for ST-elevation myocardial infarction patients presenting with severe and profound cardiogenic shock: the Academic Medical Center intensive care unit experience. Crit Care Med 2011; 39(9):2072-2079.

24. De Backer D. Choosing catecholamine therapy for shock. Neth J Crit Care 2011; 15(6):269-275.

25. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, et al. . Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results of a randomised, open-label trial. Lancet 2013; 382(9905):1638-1645.

26. Ohman EM, George BS, White CJ, Kern MJ, Freedman RJ, Lundergan C, et al. Use of aortic counterpulsation to improve coronary artery patency during acute myocardial infarction: Results of a randomized trial. The Randomized IABP Study Group. Circulation 1994; 90(2):792-799.

27. Stone GW, Marsalese D, Brodie BR, Donohue B, Costantini C, Balestrini C, et al. A prospective, randomized evaluation of prophylactic intraaortic balloon counterpulsation in high risk patients with acute myocardial infarction treated with primary angioplasty. Second Primary Angioplasty in Myocardial Infarction (PAMI-II) Trial Investigators. J Am Coll Cardiol 1997; 29(7):1459-1467.

28. Van 't Hof AW, Liem AL, de Boer MJ, Hoorntje JC, Suryapranata H, Zijlstra F. A randomized comparison of intra-aortic balloon pumping after primary coronary angioplasty in high risk patients with acute myocardial infarction. Eur Heart J 1999; 20(9):659-665.

29. Vijayalakshmi K, Kunadian B, Whittaker VJ, Wright RA, Hall JA, Sutton A, et al. . Intra-aortic counterpulsation does not improve coronary flow early after PCI in a high-risk group of patients: observations from a randomized trial to explore its mode of action. J Invasive Cardiol 2007; 19(8):339-346.

30. Gu J, Hu W, Xiao H, Feng X, Song Z, Chen Y, et al. . Prophylactic intra-aortic balloon pump reduces C-reactive protein levels and early mortality in high-risk patients undergoing percutaneous coronary intervention. Acta Cardiol 2011; 66(4):499-504.

31. Ohman EM, Nanas J, Stomel RJ, Leesar MA, Nielsen DW, O'Dea D, et al. Thrombolysis and counterpulsation to improve survival in myocardial infarction complicated by hypotension and suspected cardiogenic shock or heart failure: results of the TACTICS trial. J Thromb Thrombolysis 2005; 19(1):33-39.