Circulation

ORIGINAL RESEARCH ARTICLE

Intraaortic Balloon Pump in Cardiogenic Shock Complicating Acute Myocardial Infarction

Long-Term 6-Year Outcome of the Randomized IABP-SHOCK II Trial

Holger Thiele, MD
Uwe Zeymer, MD
Nathalie Thelemann, MD
Franz-Josef Neumann, MD
Jörg Hausleiter, MD
Mohamed Abdel-Wahab, MD
Roza Meyer-Saraei, PhD
Georg Fuernau, MD
Ingo Eitel, MD
Rainer Hambrecht, MD
Michael Böhm, MD
Karl Werdan, MD
Stephan B. Felix, MD
Marcus Hennersdorf, MD
Steffen Schneider, PhD
Taoufik Ouarrak, PhD
Steffen Desch, MD
Suzanne de Waha-Thiele, MD
On behalf of the IABP-SHOCK II Trial (Intraaortic Balloon Pump in Cardiogenic Shock II) Investigators*

BACKGROUND: The role of intraaortic balloon counterpulsation (IABP) in cardiogenic shock is still a subject of intense debate despite the neutral results of the IABP-SHOCK II trial (Intraaortic Balloon Pump in Cardiogenic Shock II) with subsequent downgrading in international guidelines. So far, randomized data on the impact of IABP on long-term clinical outcomes in patients with cardiogenic shock complicating acute myocardial infarction are lacking. Furthermore, only limited evidence is available on general long-term outcomes of patients with cardiogenic shock treated by contemporary practice.

METHODS: The IABP-SHOCK II trial is a multicenter, randomized, open-label trial. Between 2009 and 2012, 600 patients with cardiogenic shock complicating acute myocardial infarction undergoing early revascularization were randomized to IABP versus control.

RESULTS: Long-term follow-up was performed 6.2 years (interquartile range 5.6–6.7) after initial randomization. Follow-up was completed for 591 of 600 patients (98.5%). Mortality was not different between the IABP and the control group (66.3% versus 67.0%; relative risk, 0.99; 95% CI, 0.88–1.11; P=0.98). There were also no differences in recurrent myocardial infarction, stroke, repeat revascularization, or rehospitalization for cardiac reasons (all P>0.05). Survivors' quality of life as assessed by the EuroQol 5D questionnaire and the New York Heart Association class did not differ between groups.

CONCLUSIONS: IABP has no effect on all-cause mortality at 6-year long-term follow-up. Mortality is still very high, with two thirds of patients with cardiogenic shock dying despite contemporary treatment with revascularization therapy.

CLINICAL TRIAL REGISTRATION: URL: https://clinicaltrials.gov/. Unique identifier: NCT00491036.

*IABP-SHOCK II Investigators are listed in the Appendix.

Key Words: acute myocardial infarction ■ angioplasty ■ assist device ■ cardiogenic shock ■ intraaortic balloon counterpulsation

Sources of Funding, see page XXX

https://www.ahajournals.org/journal/circ

Clinical Perspective

What Is New?

- The long-term effects of intraaortic balloon pump (IABP) assessed at 6 years in patients with acute myocardial infarction complicated by cardiogenic shock on all-cause mortality have been assessed.
- There were no relevant differences in long-term outcome and other secondary end points between patients randomized to IABP or control.
- Quality of life and functional status were similar at long-term follow-up.

What Are the Clinical Implications?

- The current long-term follow-up of the IABP-SHOCK II trial (Intraaortic Balloon Pump in Cardiogenic Shock II) did not show an effect of IABP on mortality in patients with cardiogenic shock supporting current guideline recommendations to not routinely use IABP.

Short- to midterm mortality in cardiogenic shock complicating acute myocardial infarction remains high at rates between 40% and 60%.[1–6] Intraaortic balloon pumping (IABP) has been the most widely used mechanical hemodynamic support device for ≈5 decades.[6] Experimental and registry trials suggested an augmentation of the diastolic blood pressure, thereby improving coronary perfusion with a small but significant effect on cardiac output.[7] However, in a small randomized trial, these effects on cardiac output were not different to those observed in the control group.[8] Based on the subsequent IABP-SHOCK II trial (Intraaortic Balloon Pump in Cardiogenic Shock II), which did not show a benefit of IABP use versus control on 30-day and 1-year mortality,[9,10] European guidelines downgraded IABP use for cardiogenic shock from a previous class I to a class III B recommendation.[11–13] In the US guidelines, IABP use has been downgraded to a class IIb B recommendation based on registry data.[14,15]

In elective high-risk percutaneous coronary intervention (PCI), IABP showed no benefit at short-term follow-up but suggested a significant mortality reduction at 5-year follow-up.[16,17] So far, randomized data on the impact of IABP on long-term clinical outcomes in patients with cardiogenic shock complicating acute myocardial infarction are lacking. Furthermore, only limited evidence is available on general long-term outcomes of cardiogenic shock patients treated by contemporary practice.[18]

Therefore, we performed a long-term follow-up of the IABP-SHOCK II trial to assess differences in clinical outcome between IABP and control, predictors of cardiogenic shock mortality, effects on quality of life, and functional status.

METHODS

Study Design

The trial design of the randomized, open-label, multicenter IABP-SHOCK II trial and the 30-day and 12-month results, including the primary end point have been previously published.[9,10,19] In brief, this investigator-initiated trial was performed at 37 German centers and coordinated by the Heart Center Leipzig at the University of Leipzig, Germany, and the Institut für Herzinfarktforschung, Ludwigshafen, Germany, a clinical research organization. The main inclusion criterion was cardiogenic shock with planned early revascularization preferably by PCI. Cardiogenic shock was defined by typical criteria with the presence of systemic hypotension, pulmonary congestion, and signs of impaired organ perfusion. Exclusion criteria were resuscitation >30 minutes, no intrinsic heart action, severe cerebral deficit, mechanical causes of cardiogenic shock, onset of shock >12 hours, severe peripheral artery disease precluding IABP insertion, aortic regurgitation >grade 2, >90 years of age, shock of other cause, and other severe concomitant disease with a limited life expectancy of <6 months.

The study was approved by national regulatory authorities and ethics committees of all participating centers. Additional ethical approval was obtained for the extended long-term follow-up. The trial complied with the Declaration of Helsinki and is registered at www.clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT00491036). Informed consent at randomization was obtained using a previously validated and dedicated informed consent process.[10,19] The trial organization included an independent data safety monitoring board and a steering committee responsible for trial conduct. The first and senior authors had full access to all the data in the study and take responsibility for its integrity and data analysis. The data, analytic methods, and study materials cannot be made available to other researchers for purposes of reproducing the results or replicating the procedure because the trial was started long before the general introduction of the data-sharing concept, and informed consent did not incorporate such policy.

Randomization, Treatment, and Long-Term Follow-up

Between June 2009 and March 2012, 600 patients were randomized with a 1:1 ratio in an open-label fashion to IABP (n=301) or control (n=299) using an internet-based program. By protocol, crossover to IABP in controls was only allowed for patients developing a mechanical complication. All other treatment was similar between groups and followed specific guideline recommendations.[20] Thus, the only difference in treatment between groups was IABP support.

For the assessment of clinical outcome at 6 years, all-cause mortality was determined based on data of the German national death registry, which is a noncentralized registry run by each German commune. In survivors, a structured telephone interview with interviewers masked to treatment allocation was performed. Any clinical event was verified by hospital or general practitioner records.

End Points

In addition to the primary study end point 30-day all-cause mortality,[10] mortality at 6 and 12 months was assessed by

protocol.[9,19] The current long-term follow-up was added as an amendment to the original study protocol. All-cause mortality, reinfarction using the third universal definition of myocardial infarction definition,[21] revascularization by either PCI or coronary artery bypass grafting, stroke, and implantable cardioverter defibrillator implantation were assessed.

At 6-year follow-up, symptoms of heart failure using the New York Heart Association classification and angina using the Canadian Cardiovascular Society classification were assessed in all survivors in addition to quality of life using the EuroQol (EQ)-5D-3 L (www.euroqol.org) questionnaire. This questionnaire has been described and reported previously at 12-month follow-up.[9] In brief, it is a descriptive system of health-related quality-of-life states consisting of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), each of which can take 1 of 3 responses (no problems, some or moderate problems, or extreme problems). In addition, the EQ visual analogue scale was obtained assessing the self-rated health on a scale from 0 to 100. Results are displayed as EQ-5D-3 L index value with 1 indicating best quality of life and the EQ visual analogue scale with 100 indicating the best subjective health status.

The safety end points of bleeding, sepsis, and peripheral ischemic vascular complication were only assessed for the initial hospital phase for ≤30 days. Further safety analyses were only performed for stroke.[10,19]

Statistical Analysis

The initial study was powered to detect a 12% absolute difference for the primary end point of 30-day mortality, assuming a mortality rate of 56% in the control arm and 44% in the IABP arm. Accounting for 2 interim analyses and a 2% dropout rate, 600 patients were recruited.[10,19] There was no formal power analysis for the long-term follow-up. All data were analyzed according to the intention-to-treat principle, with an additional sensitivity analysis according to the per-protocol and as-treated population for the evaluation of data robustness.

Survival times were calculated as time from randomization to time of death or last known follow-up. Log-rank testing was used to analyze continuous survival times, and the χ^2 test was used to compare mortality rates.

Other end points were assessed by Fisher's or χ^2test for binary and Mann–Whitney *U* test for continuous secondary end points to compare both treatment arms.

Cox proportional hazards regression modeling was used to identify independent clinical and laboratory risk factors at baseline associated with mortality. All baseline variables related to mortality on univariable analysis (defined by $P<0.10$) were further analyzed in a stepwise multivariable model. The same previously predefined subgroup analyses were applied for sex, age (<50 years, 50–75 years, >75 years), diabetes mellitus (yes/no), arterial hypertension (yes/no), ST-elevation versus non-ST-elevation myocardial infarction, anterior versus nonanterior myocardial infarction, and previous myocardial infarction (yes/no). Previous post hoc subgroups such as hypothermia versus no hypothermia and baseline blood pressure <80 mm Hg versus ≥80 mm Hg were once again evaluated. The Breslow–Day test was used for analyzing the interaction of treatment assignment and subgroup factors.

A 2-tailed *P* value <0.05 was considered significant. Statistical analyses were performed with SAS statistical package, version 9.4 (SAS Institute).

RESULTS

Patients, Procedures, and Follow-Up

From 790 initially screened cardiogenic shock patients, 600 patients were randomized to IABP (n=301) or control (n=299). Revascularization status, study protocol compliance, and follow-up at 30 days, 6 months, 12 months, and 6 years are displayed in Figure 1. The long-term follow-up was performed a median of 6.2 years (interquartile range, 5.6–6.7) after initial randomization. Follow-up was complete for 591 (98.5%) of the 600 patients. Baseline characteristics were well balanced between treatment groups.[10] The median age at randomization was 70 years (interquartile range, 58–77), and more than two thirds were male. The median duration of IABP support was 3.0 days (interquartile range, 2.0–4.0, with a range of 1–16 days). IABP placement was performed in 86.6% after revascularization.

Clinical Outcome

There was no significant difference in mortality between the IABP group compared with control at 6-year follow-up after randomization (66.3% versus 67.0%; relative risk, 0.99; 95% CI, 0.88–1.11; *P*=0.98) (Table 1). The corresponding Kaplan–Meier curves are shown in Figure 2. For the long-term follow-up, only minor variation occurred in the relative risk estimates when analyses were restricted to the per-protocol (65.2% versus 67.6%; relative risk, 0.96; 95% CI, 0.85–1.08; *P*=0.83) and as-treated (65.8% versus 67.6%; relative risk, 0.97; 95% CI 0.87–1.09; *P*=0.50) (Figure I in the online-only Data Supplement) populations. Subgroup analyses confirmed the consistency of the results among all predefined and post hoc subgroups (Figure 3). For patients in the IABP group, there was no significant difference in long-term mortality between the 13.4% undergoing IABP insertion before revascularization (64.9%) and the 86.6% after revascularization (64.6%; *P*=0.97). For patients with low, intermediate, and high risk based on the IABP-SHOCK II score,[22] long-term mortality was 48.7%, 77.8%, and 90.6%, respectively. There were no differences between the 2 treatment groups based on the risk categories.

Multivariable modeling revealed increasing age, history of stroke, baseline arterial lactate, creatinine level, oliguria (<30 mL/h), multivessel coronary artery disease, cold or clammy skin and extremities, and left bundle-branch block at admission as independent risk factors for mortality (Table 2). IABP treatment was not predictive of survival.

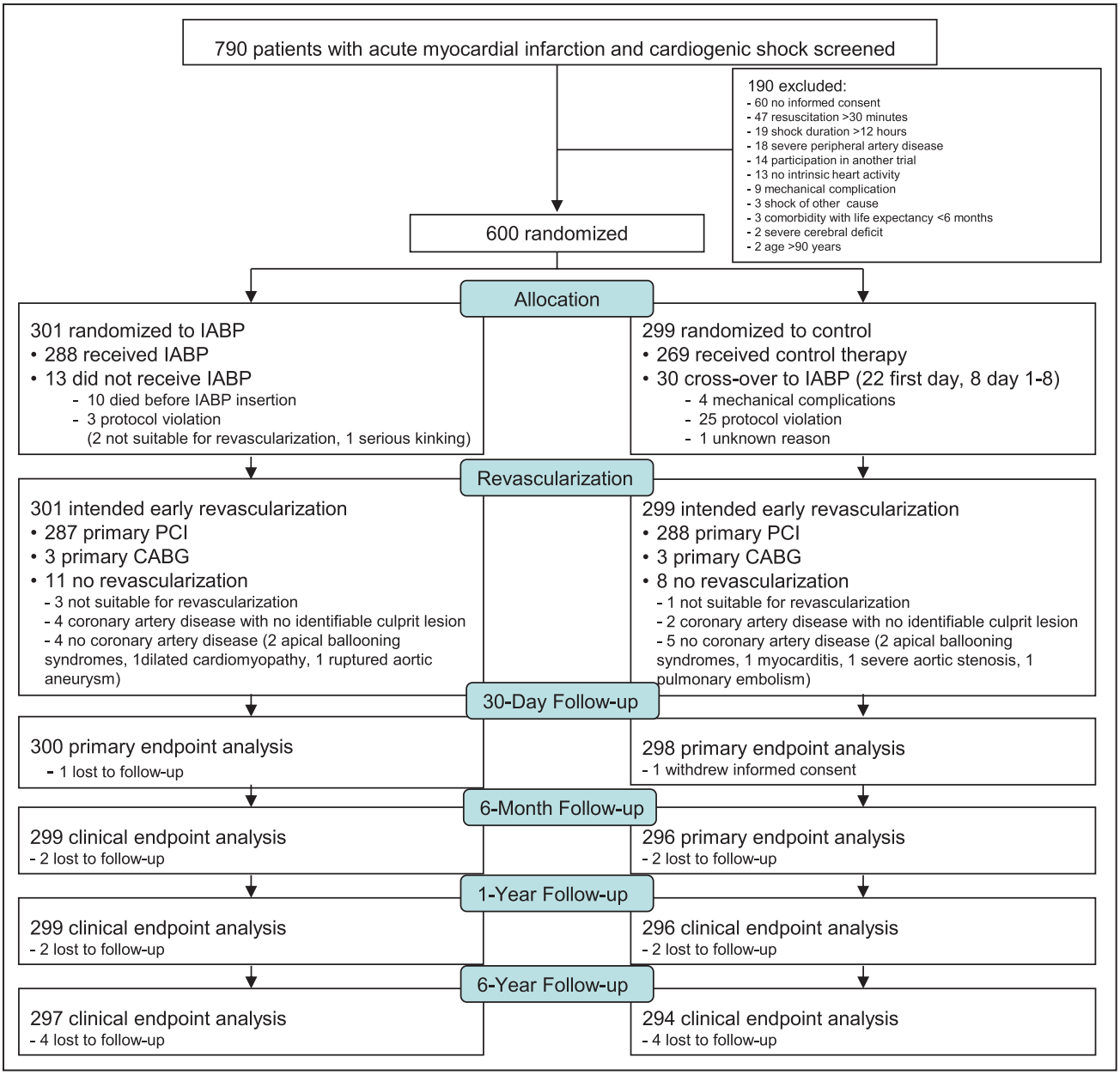

Figure 1. Trial flow.
Screening, randomization, revascularization, management strategy, and follow-up at 30 days, 6 months, 12 months, and 6 years. CABG indicates coronary artery bypass grafting; IABP, intraaortic balloon pump; and PCI, percutaneous coronary intervention.

There were no significant differences in recurrent infarction, stroke, requirement for internal cardioverter defibrillator, or additional revascularization procedures at 6-year follow-up (Table 1).

Functional Status and Quality of Life

Among 6-year survivors (n=197), 82% were in New York Heart Association class I or II (82% in the IABP and 82% in the control group; *P*=1.00). The overall rate of angina was low. In total, 13% in the IABP group versus 25% in the control group were in Canadian Cardiovascular Society class I or II (*P*=0.06). The EQ-5D-3 L index value was assessed for 173 survivors (88%), with 0.8 indicating moderate to good quality of life. There were no differences in quality-of-life assessment between both treatment groups with respect to the 5 quality-of-life dimensions and the EQ visual analogue scale (Figure IIA and IIB in the online-only Data Supplement).

DISCUSSION

In this randomized trial of patients with cardiogenic shock complicating acute myocardial infarction, IABP support did not result in a 6-year survival benefit compared with control, supporting the short-term 30-day

Table 1. Clinical Outcomes at 6 Years

Variable	Intraaortic Balloon Pump (n=297)	Control (n=294)	Relative Risk (95% CI)	*P* Value
All-cause mortality	197/297 (66.3)	197/294 (67.0)	0.99 (0.88–1.11)	0.98
Events in 6-year survivors				
Reinfarction	9/100 (9.0)	7/97 (7.2)	1.25 (0.48–3.22)	0.65
Stroke	1/100 (1.0)	6/97 (6.2)	0.16 (0.02–1.32)	0.06
Recurrent revascularization	26/100 (26.0)	31/97 (32.0)	0.81 (0.52–1.26)	0.36
Repeat percutaneous coronary intervention	18/100 (18.0)	26/97 (26.8)	0.67 (0.39–1.14)	0.14
Additional coronary artery bypass grafting	8/100 (8.0)	7/97 (7.2)	1.11 (0.42–2.94)	0.84
Implantable cardioverter defibrillator implantation	13/100 (13.0)	15/97 (15.5)	0.84 (0.42–1.67)	0.62

Values indicate n/total (%).

and midterm 1-year data. In addition to mortality, there were also no benefits of IABP on other secondary outcome variables. Despite early revascularization in all patients and optimal guideline-adherent medical therapy, mortality remains high, with more than two thirds of patients dying at 6-year follow-up. However, a relevant portion of survivors report no or mild symptoms with respect to New York Heart Association and Canadian Cardiovascular Society class with a moderate to good quality of life.

IABP has been in clinical use for ≈5 decades,[23] largely on the basis of observational data as well as the belief in a beneficial effect on coronary blood flow, myocardial oxygen demand, and afterload reduction.[7] The widespread use of IABP in cardiogenic shock had been at odds with the paucity of adequately powered randomized controlled trials in this setting. After publication of the IABP-SHOCK II trial, IABP use has been downgraded in guidelines with a parallel decline in clinical practice.[11,13,24–26] Similar to cardiogenic shock, data are sparse for IABP in elective high-risk PCI, with only 1 randomized trial in this setting, which also showed no benefit of IABP on major adverse cardiac and cardiovascular events at 28 days in patients with severe left ventricular dysfunction and extensive coronary disease.[16] In this trial, there was a mortality benefit at longer 5-year follow-up.[17] However, there was a lack of information on possible mechanisms supporting this observed mortality reduction with IABP support in this population, given the absence of death etiology and lack of data on left ventricular function and remodeling. As such, the finding of a mortality benefit may be a play of chance in this trial. In the current long-term follow-up of IABP-SHOCK II, results were consistent with respect to a lack of benefit at short-, mid, and long-term follow-up.

There are multiple possible explanations for this lack of benefit. In the IABP-SHOCK I randomized pilot trial, no differences between IABP and control were observed

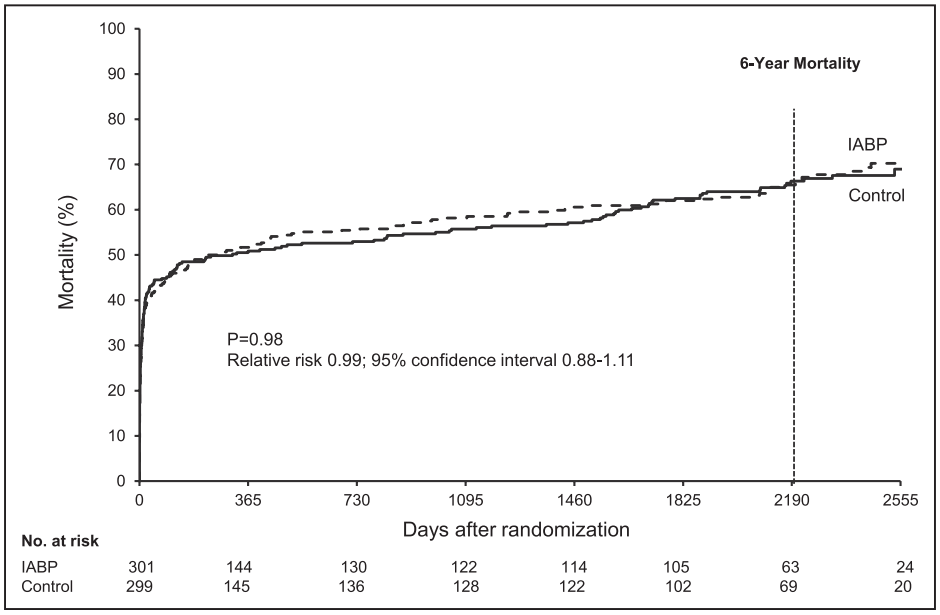

Figure 2. Time-to-event curves through 6 years.
Time-to-event curves through 6 years for all-cause mortality. *P* value is based on the log-rank test. Event rates represent Kaplan–Meier estimates. IABP indicates intraaortic balloon pump.

Baseline Variable	N	6-Year Mortality n (%) IABP	Control	Relative Risk (95% CI)	P-Value for Interaction
Female	184	67 (69.1)	64 (73.6)	0.94 (0.78-1.13)	0.51
Male	407	130 (65.0)	133 (64.3)	1.01 (0.88-1.17)	
Age <50 years	70	15 (41.7)	20 (58.8)	0.71 (0.44-1.14)	0.32
Age 50-75 years	347	102 (61.4)	108 (59.7)	1.02 (0.87-1.22)	
Age >75 years	174	80 (84.2)	69 (87.3)	0.96 (0.85-1.09)	
Diabetes	194	74 (71.2)	73 (81.1)	1.04 (0.90-1.22)	0.10
No diabetes	393	120 (63.5)	124 (60.8)	1.05 (0.85-1.30)	
History of hypertension	408	153 (72.5)	137 (69.5)	1.04 (0.92-1.18)	0.08
No history of hypertension	178	40 (49.4)	60 (61.9)	0.80 (0.61-1.05)	
STEMI/LBBB	412	132 (66.0)	138 (65.1)	1.01 (0.88-1.17)	0.48
NSTEMI	179	65 (67.0)	59 (72.0)	0.93 (0.77-1.13)	
Anterior STEMI	215	73 (65.2)	69 (67.0)	0.97 (0.80-1.18)	0.56
Non-anterior STEMI	197	59 (67.1)	69 (63.3)	1.06 (0.86-1.30)	
Previous infarction	130	57 (80.3)	43 (72.9)	1.10 (0.91-1.34)	0.22
No previous infarction	460	140 (62.2)	154 (65.5)	0.95 (0.83-1.10)	
Hypothermia	222	65 (62.5)	81 (68.6)	0.91 (0.75-1.20)	0.28
No hypothermia	369	132 (68.4)	116 (65.9)	1.04 (0.90-1.20)	
Blood pressure <80 mmHg	160	54 (70.1)	63 (75.9)	0.92 (0.76-1.11)	0.35
Blood pressure ≥80 mmHg	425	142 (65.4)	132 (63.5)	1.03 (0.90-1.19)	

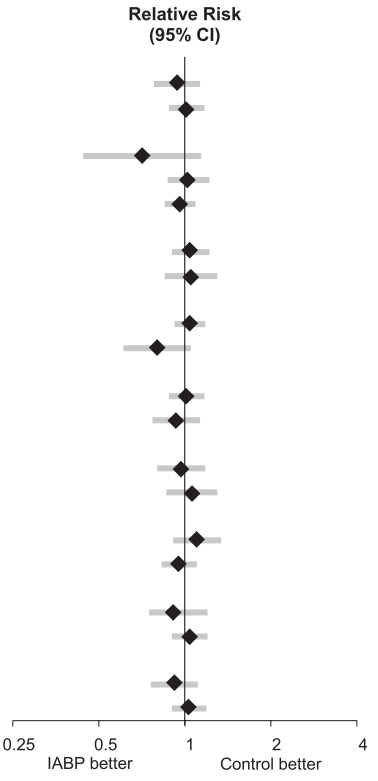

Figure 3. Forest plot subgroup analyses for all patients with 6-year follow-up.
The forest plots indicate relative risk and 95% CIs for predefined subgroups and the post hoc subgroups hypothermia versus no hypothermia and baseline systolic blood pressure <80 mm Hg versus ≥80 mm Hg. IABP indicates intraaortic balloon pump; LBBB, left bundle-branch block; NSTEMI, non-ST-elevation myocardial infarction; and STEMI, ST-elevation myocardial infarction.

in any of the measured hemodynamic parameters.[8] In the subsequent large IABP-SHOCK II trial, there were no effects on markers of systemic inflammation, arterial lactate, renal function, mean arterial blood pressure, intensive care unit scores, or doses of catecholamines, thereby providing supportive pathophysiological explanations for any lack of mortality benefit.[10] The results were also remarkably consistent for all subgroups studied in the shorter and current long-term follow-up. Furthermore, the results with this long-term follow-up are in line with previous registry data and 2 small randomized trials using fibrinolysis or PCI, which were all negative.[8,15,27]

In the current long-term follow-up trial, there was an additional absolute mortality increase of ≈28% at 6 years compared with the 30-day results. This difference is slightly higher, but overall mortality rates are nearly identical compared with the SHOCK trial (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock), the only other large randomized cardiogenic shock trial reporting a 6-year long-term follow-up, which had mortality rates of 46.7% at 30 days and 67.2% at 6 years in the early revascularization strategy.[18,28,29] These data confirm once again, as also shown recently in the CULPRIT-SHOCK trial (Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock),[4,5] that mortality or differences in mortality in cardiogenic shock are determined to a greater extent by the first 30 days. However, the risk of death is still substantial after the acute phase. Any possible improvement in mortality over time may be counterbalanced by increasing patient age and also more patients experiencing resuscitation before hospital admission. For these survivors, additional intensified medical and possibly interventional therapy may be required.

Quality of life and the functional status for survivors were relatively good. Similar to the SHOCK trial and the 1-year data of the CULPRIT-SHOCK trial, ≈90% of survivors were in New York Heart Association class I or II.[4,28] The more detailed quality-of-life assessment in the current trial using a standardized questionnaire showed health-related quality-of-life states being comparable to a general population survey.[30]

There is wide range in the risk of death for patients with cardiogenic shock complicating myocardial infarction.[22] An objective score to assess the mortality risk for individual patients has been derived from the IABP-SHOCK II population, which has been validated internally and externally.[22] The current results confirm that the readily available baseline arterial lactate, indicating the severity of end organ perfusion abnor-

Table 2. Predictors of 6-Year Mortality in Univariable and Stepwise Multivariable Cox Regression Analysis

Variable	Univariable		Stepwise Multivariable	
	Hazard Ratio (95% CI)	*P* Value	Hazard Ratio (95% CI)	*P* Value
Altered mental status	1.37 (1.08–1.74)	0.009	–	–
Mechanical ventilation	1.00 (0.82–1.22)	0.99	–	–
Current smoking	0.68 (0.54–0.84)	<0.001	–	–
History of arterial hypertension	1.41 (1.12–1.77)	0.003	–	–
Hemoglobin, mmol/l	0.87 (0.81–0.93)	<0.001	–	–
Hematocrit, %	0.11 (0.03–0.42)	0.001	–	–
Sinus rhythm	0.72 (0.57–0.90)	0.005	–	–
ST-elevation myocardial infarction	0.76 (0.62–0.94)	0.01	–	–
pH <7.36 at admission	1.37 (1.11–1.69)	0.004	–	–
Age, per 10 y	1.39 (1.27–1.52)	<0.001	1.33 (1.20–1.47)	<0.001
History of stroke	1.99 (1.41–2.80)	<0.001	1.52 (1.06–2.05)	0.02
Baseline arterial lactate, per 10 mmol/l	2.79 (2.22–3.51)	<0.001	2.68 (2.06–3.49)	<0.001
Baseline creatinine, per 100 µmol/l	1.03 (1.02–1.04)	<0.001	1.02 (1.00–1.03)	0.004
Oliguria (<30 mL/h)	1.68 (1.36–2.06)	<0.001	1.28 (1.01–1.62)	0.04
Multivessel coronary artery disease	1.37 (1.17–1.52)	<0.001	1.28 (1.05–1.46)	0.02
Cold, clammy skin and extremities	1.49 (1.11–2.00)	0.008	1.48 (1.06–2.05)	0.02
Left bundle-branch block	1.99 (1.53–2.60)	<0.001	1.52 (1.13–2.03)	0.005

Baseline patient variables related to mortality on univariable analysis defined by a *P* value <0.10. The first 9 variables initially entered into the model were not independently associated with mortality in the stepwise multivariable model.

malities, is 1 of the strongest predictors of long-term mortality. Baseline arterial lactate, together with age and oliguria, should therefore be integrated in mortality risk assessment in clinical practice and may also guide decision management for mechanical circulatory support.[6]

This long-term follow-up study has some strengths, including its size, multicenter design, recruitment of a high-risk real-world cardiogenic shock population, and near complete clinical follow-up. There are also some limitations, such as the lack of blinding, which is because of the nature of the intervention. Given the low number of surgically treated patients, the IABP effects might not be generalizable to patients undergoing immediate bypass surgery.

In conclusion, this randomized, multicenter trial confirmed that in patients with cardiogenic shock complicating myocardial infarction undergoing early revascularization, IABP support does not reduce 6-year long-term mortality. Cardiogenic shock mortality has virtually not changed since the introduction of early revascularization >2 decades ago. For the one third of survivors at 6 years functional outcome as well as quality of life is good.

ARTICLE INFORMATION

Received October 1, 2018; accepted October 11, 2018.

The online-only Data Supplement is available with this article at https://www.ahajournals.org/doi/suppl/10.1161/CIRCULATIONAHA.118.038201.

Correspondence

Holger Thiele, MD, Department of Internal Medicine/Cardiology, Heart Center Leipzig, University of Leipzig, Strümpellstraße 39, 04289 Leipzig, Germany. Email holger.thiele@medizin.uni-leipzig.de

Affiliations

Heart Center Leipzig, University of Leipzig, Germany (H.T., M.A.-W., S.D.). Leipzig Heart Institute, Germany (H.T., M.A.-W., S.D.). Klinikum Ludwigshafen and Institut für Herzinfarktforschung, Germany (U.Z., S.S., T.O.). University Heart Center, Luebeck, Germany (N.T., R.M.-S., G.F., I.E., S.d.W.-T.). Heart Center Bad Krozingen, University of Freiburg, Germany (F.-J.N.). Klinikum der Ludwig-Maximilians, Universität München, Germany (J.H.). Heart Center, Segeberger Kliniken, Bad Segeberg, Germany (M.A.-W.). German Center for Cardiovascular Research, Partner Site Hamburg/Kiel/Luebeck, Luebeck (G.F., I.E., S.D., S.d.W.-T.). Klinikum Links der Weser, Bremen, Germany (R.H.). University Clinic of Saarland, Homburg/Saar, Germany (M.B.). Department of Internal Medicine/Cardiology, Martin-Luther University Halle-Wittenberg, Germany (K.W.). University Medicine Greifswald, Germany (S.B.F.). Department of Internal Medicine/Cardiology, SLK Kliniken Heilbronn, Germany (M.H.).

Acknowledgments

The authors thank the patients who agreed to participate in this trial, the study contributors, and the investigators recruiting patients.

Sources of Funding

This work was supported by the German Research Foundation, German Heart Research Foundation, German Cardiac Society, Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte, and Heart Center Leipzig at University of Leipzig, as well as unrestricted grants from Maquet Cardiopulmonary AG, Hirrlingen, Germany, and Teleflex Medical, Everett, MA.

Disclosures

None.

APPENDIX

IABP-SHOCK II Investigators: Zehra Alkisoglu, Ferenc Follath, Sonja Frey, Johannes Haerting, Kurt Huber, Bernhard Maisch, Beate Messemer, Taoufik Ourrak, Steffen Schneider, Gerhard Schuler, Holger Thiele, Karin Vonderschmitt, Karl Werdan, and Uwe Zeymer.

REFERENCES

1. Aissaoui N, Puymirat E, Tabone X, Charbonnier B, Schiele F, Lefevre T, Durand E, Blanchard D, Simon T, Cambou J-P, Danchin N. Improved outcome of cardiogenic shock at the acute stage of myocardial infarction: a report from the USIK 1995, USIC 2000, and FAST-MI French Nationwide Registries. *Eur Heart J*. 2012;33:2535–2543.
2. Goldberg RJ, Spencer FA, Gore JM, Lessard D, Yarzebski J. Thirty-year trends (1975 to 2005) in the magnitude of, management of, and hospital death rates associated with cardiogenic shock in patients with acute myocardial infarction: a population-based perspective. *Circulation*. 2009;119:1211–1219.
3. Jeger RV, Radovanovic D, Hunziker PR, Pfisterer ME, Stauffer JC, Erne P, Urban P; AMIS Plus Registry Investigators. Ten-year trends in the incidence and treatment of cardiogenic shock. *Ann Intern Med*. 2008;149:618–626.
4. Thiele H, Akin I, Sandri M, de Waha-Thiele S, Meyer-Saraei R, Fuernau G, Eitel I, Nordbeck P, Geisler T, Landmesser U, Skurk C, Fach A, Jobs A, Lapp H, Piek JJ, Noc M, Goslar T, Felix SB, Maier LS, Stepinska J, Oldroyd K, Serpytis P, Montalescot G, Barthelemy O, Huber K, Windecker S, Hunziker L, Savonitto S, Torremante P, Vrints C, Schneider S, Zeymer U, Desch S. One-year outcomes after PCI strategies in cardiogenic shock [published online ahead of print August 25, 2018]. *N Engl J Med*. doi: 10.1056/NEJMoa1808788
5. Thiele H, Akin I, Sandri M, Fuernau G, de Waha S, Meyer-Saraei R, Nordbeck P, Geisler T, Landmesser U, Skurk C, Fach A, Lapp H, Piek JJ, Noc M, Goslar T, Felix SB, Maier LS, Stepinska J, Oldroyd K, Serpytis P, Montalescot G, Barthelemy O, Huber K, Windecker S, Savonitto S, Torremante P, Vrints C, Schneider S, Desch S, Zeymer U; CULPRIT-SHOCK Investigators. PCI strategies in patients with acute myocardial infarction and cardiogenic shock. *N Engl J Med*. 2017;377:2419–2432. doi: 10.1056/NEJMoa1710261
6. Thiele H, Ohman EM, Desch S, Eitel I, de Waha S. Management of cardiogenic shock. *Eur Heart J*. 2015;36:1223–1230. doi: 10.1093/eurheartj/ehv051
7. Scheidt S, Wilner G, Mueller H, Summers D, Lesch M, Wolff G, Krakauer J, Rubenfire M, Fleming P, Noon G, Oldham N, Killip T, Kantrowitz A. Intra-aortic balloon counterpulsation in cardiogenic shock: report of a co-operative clinical trial. *N Engl J Med*. 1973;288:979–984. doi: 10.1056/NEJM197305102881901
8. Prondzinsky R, Unverzagt S, Russ M, Lemm H, Swyter M, Wegener N, Buerke U, Raaz U, Ebelt H, Schlitt A, Heinroth K, Haerting J, Werdan K, Buerke M. 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;37:378–384. doi: 10.1097/SHK.0b013e31824a67af
9. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, de Waha A, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Lauer B, Böhm M, Ebelt H, Schneider S, Werdan K, Schuler G; Intraaortic Balloon Pump in cardiogenic shock II (IABP-SHOCK II) trial investigators. 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;382:1638–1645. doi: 10.1016/S0140-6736(13)61783-3
10. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Fuhrmann J, Böhm M, Ebelt H, Schneider S, Schuler G, Werdan K; IABP-SHOCK II Trial Investigators. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med*. 2012;367:1287–1296. doi: 10.1056/NEJMoa1208410
11. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimský P. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the task force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018;39:119–177.
12. Neumann FJ, Sousa Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Jüni P, Kastrati A, Koller A, Kristensen SD, Niebauer J, Richter DJ, Seferovic PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO. 2018 ESC/EACTS guidelines on myocardial revascularization [published online ahead of print December 18August 23, 2018]. *Eur Heart J*. doi: 10.1093/eurheartj/ehy394.
13. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P; ESC Scientific Document Group. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016;37:2129–2200. doi: 10.1093/eurheartj/ehw128
14. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX, Anderson JL, Jacobs AK, Halperin JL, Albert NM, Brindis RG, Creager MA, DeMets D, Guyton RA, Hochman JS, Kovacs RJ, Kushner FG, Ohman EM, Stevenson WG, Yancy CW; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;127:e362–e425. doi: 10.1161/CIR.0b013e3182742cf6
15. Sjauw KD, Engström AE, Vis MM, van der Schaaf RJ, Baan J Jr, Koch KT, de Winter RJ, Piek JJ, Tijssen JG, Henriques JP. 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;30:459–468. doi: 10.1093/eurheartj/ehn602
16. Perera D, Stables R, Thomas M, Booth J, Pitt M, Blackman D, de Belder A, Redwood S; BCIS-1 Investigators. Elective intra-aortic balloon counterpulsation during high-risk percutaneous coronary intervention: a randomized controlled trial. *JAMA*. 2010;304:867–874. doi: 10.1001/jama.2010.1190
17. Perera D, Stables R, Clayton T, De Silva K, Lumley M, Clack L, Thomas M, Redwood S; BCIS-1 Investigators. 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. doi: 10.1161/CIRCULATIONAHA.112.132209
18. Hochman JS, Sleeper LA, Webb JG, Dzavik V, Buller CE, Aylward P, Col J, White HD; SHOCK Investigators. Early revascularization and long-term survival in cardiogenic shock complicating acute myocardial infarction. *JAMA*. 2006;295:2511–2515. doi: 10.1001/jama.295.21.2511
19. Thiele H, Schuler G, Neumann FJ, Hausleiter J, Olbrich HG, Schwarz B, Hennersdorf M, Empen K, Fuernau G, Desch S, de Waha S, Eitel I, Hambrecht R, Böhm M, Kurowski V, Lauer B, Minden HH, Figulla HR, Braun-Dullaeus RC, Strasser RH, Rochor K, Maier SK, Möllmann H, Schneider S, Ebelt H, Werdan K, Zeymer U. Intraaortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock: design and rationale of the Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial. *Am Heart J*. 2012;163:938–945. doi: 10.1016/j.ahj.2012.03.012
20. Werdan K, Ruß M, Buerke M, Delle-Karth G, Geppert A, Schöndube FA; German Cardiac Society; German Society of Intensive Care and Emergency Medicine; German Society for Thoracic and Cardiovascular Surgery; Austrian Society of Internal and General Intensive Care Medicine; German Interdisciplinary Association of Intensive Care and Emergency Medicine; Austrian Society of Cardiology; German Society of Anaesthesiology and Intensive Care Medicine; German Society of Preventive Medicine and Rehabilitation. Cardiogenic shock due to myocardial infarction: diagnosis, monitoring and treatment: a German-Austrian S3 Guideline. *Dtsch Arztebl Int*. 2012;109:343–351. doi: 10.3238/arztebl.2012.0343
21. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; the Writing Group on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction.Third universal definition of myocardial infarction. *Eur Heart J*. 2012;33:2551–2567.
22. Pöss J, Köster J, Fuernau G, Eitel I, de Waha S, Ouarrak T, Lassus J, Harjola VP, Zeymer U, Thiele H, Desch S. Risk stratification for patients in cardiogenic shock after acute myocardial infarction. *J Am Coll Cardiol*. 2017;69:1913–1920. doi: 10.1016/j.jacc.2017.02.027

23. Kantrowitz A, Tjonneland S, Freed PS, Phillips SJ, Butner AN, Sherman JL Jr. Initial clinical experience with intraaortic balloon pumping in cardiogenic shock. *JAMA*. 1968;203:113–118.
24. Backhaus T, Fach A, Schmucker J, Fiehn E, Garstka D, Stehmeier J, Hambrecht R, Wienbergen H. Management and predictors of outcome in unselected patients with cardiogenic shock complicating acute ST-segment elevation myocardial infarction: results from the Bremen STEMI Registry. *Clin Res Cardiol*. 2018;107:371–379. doi: 10.1007/s00392-017-1192-0
25. Sandhu A, McCoy LA, Negi SI, Hameed I, Atri P, Al'Aref SJ, Curtis J, McNulty E, Anderson HV, Shroff A, Menegus M, Swaminathan RV, Gurm H, Messenger J, Wang T, Bradley SM. Use of mechanical circulatory support in patients undergoing percutaneous coronary intervention: insights from the National Cardiovascular Data Registry. *Circulation*. 2015;132:1243–1251. doi: 10.1161/CIRCULATIONAHA.114.014451
26. Shah M, Patnaik S, Patel B, Ram P, Garg L, Agarwal M, Agrawal S, Arora S, Patel N, Wald J, Jorde UP. Trends in mechanical circulatory support use and hospital mortality among patients with acute myocardial infarction and non-infarction related cardiogenic shock in the United States. *Clin Res Cardiol*. 2018;107:287–303. doi: 10.1007/s00392-017-1182-2
27. Ohman EM, Nanas J, Stomel RJ, Leesar MA, Nielsen DW, O'Dea D, Rogers FJ, Harber D, Hudson MP, Fraulo E, Shaw LK, Lee KL; TACTICS Trial. 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;19:33–39. doi: 10.1007/s11239-005-0938-0
28. Hochman JS, Sleeper LA, White HD, Dzavik V, Wong SC, Menon V, Webb JG, Steingart R, Picard MH, Menegus MA, Boland J, Sanborn T, Buller CE, Modur S, Forman R, Desvigne-Nickens P, Jacobs AK, Slater JN, LeJemtel TH; SHOCK Investigators. Should we emergently revascularize occluded coronaries for cardiogenic shock: one-year survival following early revascularization for cardiogenic shock. *JAMA*. 2001;285:190–192.
29. Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, Buller CE, Jacobs AK, Slater JN, Col J, McKinlay SM, LeJemtel TH; SHOCK Investigators. Early revascularization in acute myocardial infarction complicated by cardiogenic shock: should we emergently revascularize occluded coronaries for cardiogenic shock. *N Engl J Med*. 1999;341:625–634. doi: 10.1056/NEJM199908263410901
30. Greiner W, Claes C, Busschbach JJ, von der Schulenburg JM. Validating the EQ-5D with time trade off for the German population. *Eur J Health Econ*. 2005;6:124–130.