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CARDIOLOGY Rounds™

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Intra-aortic balloon counterpulsation in the CCU

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For the treatment of a variety of conditions seen in the CCU, intra-aortic balloon counterpulsation (IABC) is an effective intervention. IABC reduces left myocardial oxygen demand and may improve supply, and may thereby alleviate refractory myocardial ischemia. IABC may also been viewed as a pulsatile left ventricular hemodynamic assist device that augments arterial blood pressure and cardiac output. These beneficial effects are achieved with relatively infrequent serious complications. Mounting evidence from clinical trials supports the notion that the aggressive use of IABC in a number of settings results in improved patient outcomes.

Historical details

In 1958, the American cardiovascular surgeon, Dr. D. Harken, first proposed an extracorporeal pump to support the failing left ventricle.[1] His idea was to remove blood from the femoral artery during systole and to replace it rapidly during diastole. This concept was later modified at the Cleveland Clinic by Dr. S. Moulopoulos who, in 1962, demonstrated that the same hemodynamic effect could be achieved by the placement of an intravascular balloon into the aorta, whose inflation and deflation were timed to the cardiac cycle.[2] The first successful clinical application of balloon counterpulsation was reported by Dr. A. Kantrowitz in a patient with cardiogenic shock in 1968.[3] However, insertion of the intra-aortic balloon required a surgical procedure until 1980 when Bregman and Casarella described percutaneous insertion using a sheath and dilators.[4]

The design and function of the intra-aortic balloon have not changed substantially over the past 20 years. Today, the intra-aortic balloon is an intravascular, catheter-mounted counterpulsation device with a balloon volume between 30 and 50 ml.

Triggering of the IABC

After inserting the IAB in the descending aorta with its tip at the distal aortic arch (below the origin of the left subclavian artery), the balloon is connected to a drive console. The console itself consists of a pressurized gas reservoir, a monitor for ECG and pressure wave recording, and controls for adjustment of inflation/deflation timing. The gases used for inflation are either helium or carbon dioxide. The advantage of helium is its lower density and therefore, a better rapid diffusion coefficient, whereas carbon dioxide dissolves easily in blood and thereby reduces the potential consequences of gas embolization following a balloon rupture. Inflation and deflation are synchronized to the patients' cardiac cycle. Inflation at the onset of diastole results in proximal and distal displacement of blood volume in the aorta. Deflation occurs just prior to the onset of systole (Figure 1).

Physiologic effect of balloon counterpulsation - Hemodynamics

The primary goals of IABC treatment are to decrease the work of the left ventricle through afterload reduction, as well as to increase myocardial oxygen supply and decrease myocardial oxygen demand. Secondarily, IABC improves hemodynamic indices (increases

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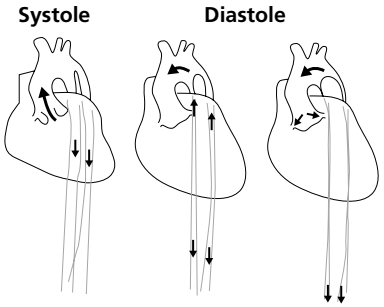
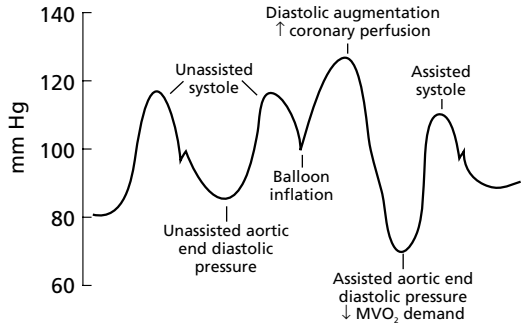
Figure 1: Placement and timing of the intra-aortic balloon pump. Inflation in diastole displaces blood proximally and distally in the aorta. Deflation at the onset of systole results in unloading the left ventricle.



Arterial waveform variations during IABC therapy

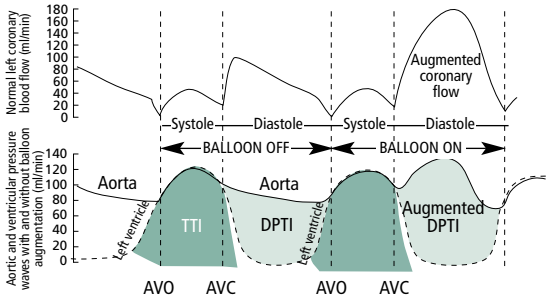


ejection fraction and cardiac output, and decreases pulmonary capillary wedge pressure and systemic vascular resistance).

Systolic wall tension is a major determinant of myocardial oxygen demand. Wall tension itself is affected by intraventricular pressure, afterload, end-diastolic volume and myocardial wall thickness. The area under the left ventricular pressure curve (the Tension-Time Index - TTI) is an important descriptor of myocardial oxygen consumption. Similarly, the integrated pressure difference between the aorta and the left ventricle during diastole (DPTI = diastolic pressure-time index) is a determinant and a descriptor of myocardial oxygen supply. Inflation of an intra-aortic balloon during diastole augments the aortic diastolic pressure and increases the gradient for coronary blood flow (DPTI). Deflation of the balloon at the onset of systole reduces impedance to left ventricular pressure and reduces systolic blood pressure and the TTI. As a result, the DPTI:TTI ratio is favourably increased (Figure 2).

The favorable reduction of left ventricular afterload will increase the cardiac index by 0.6-0.8 l/min/m^2 in most patients. Factors that may impair achieving the maximal benefit from IABC include rapid and irregular heart rhythms, excessive tachycardia, and low volume in the aorta.

Figure 2: The effect of IABC on coronary blood flow and the myocardial oxygen supply:demand ratio. TTI = Tension Time Index. DPTI = Diastolic Pressure Time Index.



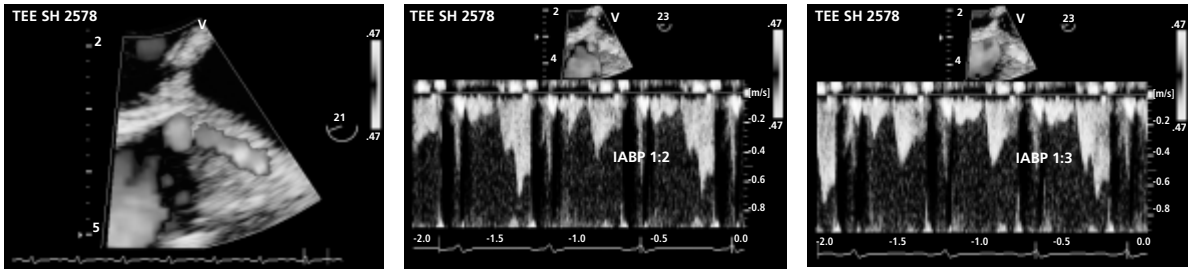
Physiologic effect of IABC – coronary blood flow

The increase in aortic root diastolic pressure achieved with inflation of the intra-aortic balloon increases coronary artery flow (Figure 3). The degree of flow augmentation is variable and depends on a patient's baseline hemodynamics. Studies by Zehetgruber, in which critically ill patients with balloon pumps in situ underwent transesophageal Doppler echocardiography to measure increased coronary blood flow in the proximal left anterior descending artery, demonstrated that patients with the lowest baseline aortic pressures and cardiac outputs achieved the greatest relative increase in coronary flow with counterpulsation.[5] Coronary flow increased by >100% in patients with the worst baseline hemodynamics, and there was no significant increase in coronary blood flow among patients with normal cardiac output.

Importantly, the observations of Zehetgruber were made only in the left anterior descending artery proximal to any hemodynamically significant stenosis. Controversy has existed surrounding the ability of IABC to increase coronary blood flow beyond stenosis, and hence result in increased perfusion of ischemic myocardium. Kern and colleagues passed small Doppler-tipped wires across tight coronary lesions and measured IABC augmented flow.[6] Despite significantly augmented flow proximal to such stenoses, there was no significant augmentation distally. An augmentation response to IABC was seen only after angioplasty of the culprit lesion. Similar findings were reported by Gurbel and colleagues who eliminated the potential confounding presence of a wire passed through a tight lesion (potentially impairing pressure transmission and flow across the stenosis) by measuring coronary flow with an epicardially placed Doppler probe in an open-chest dog model after the creation of a critical stenosis[7] (Figure 4).

An important exception to this has been demonstrated in the presence of left main, or left main-equivalent steno-

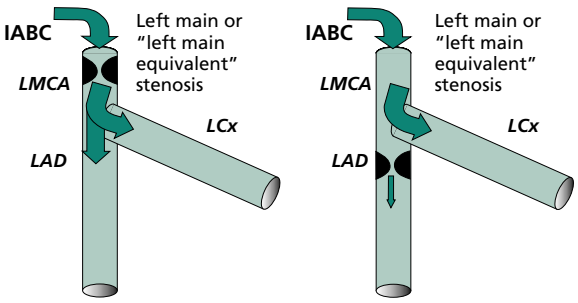
Figure 3: Coronary artery flow (velocity) recording from a female patient in profound cardiogenic shock from fulminant myocarditis. Figure 3a depicts, using colour Doppler flow-mapping (from TEE), flow in the first 2 cm of the proximal LAD. The left circumflex had a separate ostium (confirmed at angiography). Spectral flow recordings (Figures 3b and 3c) demonstrate augmentation of velocity with IABC augmentation ("A") vs native beats ("N") with 1:2 augmentation (Figure 2b) and 1:3 augmentation (Figure 3c). The same pattern was seen in the left circumflex and right coronary arteries.



sis. Hutchison and colleagues repeated measurements similar to those of Zehetgruber and found that IABC resulted in significantly increased coronary flow beyond such stenoses.[8] Possible explanations for this observation include the absence of non-obstructed branch vessels proximal to the stenosis, thereby eliminating preferential "run-off" of pressure and flow through branch vessels, and achieving pressure and flow augmentation distal to the LMS stenosis and into the ischemic myocardium. Another aspect of this study that may explain why IABC was seen to augment flow distal to LMS lesions was that the patients studied were ischemic in their anterior walls. Myocardial ischemia eliminates coronary autoregulation, and results in a direct pressure-flow relationship. Therefore, augmentation of proximal aortic pressure and proximal coronary artery pressure by IABC, results in an increase in myocardial perfusion in an ischemic territory. In the majority of all other studies of coronary flow observations and myocardial flow, the myocardial bed was non-ischemic, and therefore, less likely to have a passive pressure-flow relationship, and to achieve myocardial flow augmentation with aortic pressure augmentation from IABC or, for example, from vasopressors (Figure 5).

Despite the controversy surrounding the effects on coronary flow to ischemic myocardium, the significant improvement in myocardial oxygen demand achieved primarily through afterload reduction makes IABC a useful intervention in the setting of ischemia.

Figure 4: Figure 4a depicts IABC observed flow augmentation in the distal LMCA and LAD as has been observed with TEE recordings in patients with LMCA lesion-generated anterior wall ischemia. A potential explantion as to why flow augmentation has not been observed in many studies of IABC and its effect on myocardial flow is that in the majority of such studies, the lesion is located after branch vessels that may "vent" the augmentation effect (4b).



LAD = left anterior descending artery
LMCA = Left main coronary artery
LCx = Left circumflex artery

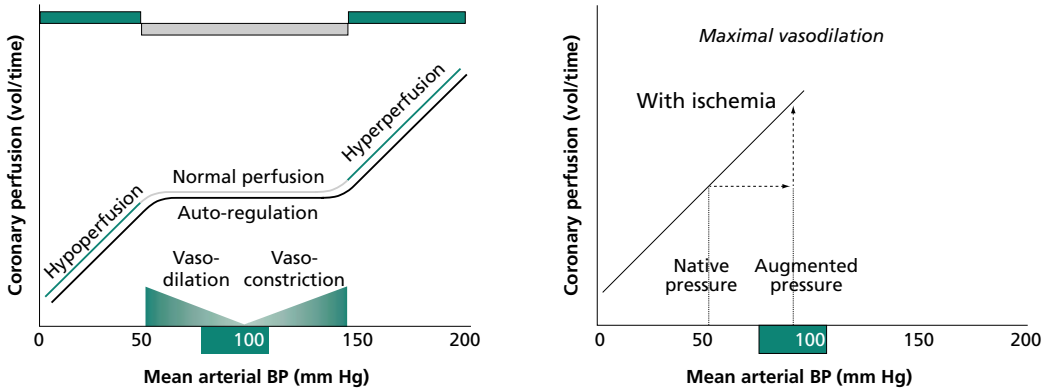
Indications, contraindications and complications

Table 1 summarizes the indications and contraindications for IABC use. The complication rate associated with IABC ranges from 12%[9]-30%[10] in reported series. In the largest prospective study published,[11] major complications occurred in 15% of patients. Death occurred in 0.5% and was due to systemic emboli, stroke, or aortic

Table 1: Indications and contraindications for IABC.

Indications	Absolute contraindications
Cardiogenic shock	Severe aortic insufficiency
Mechanical complications of AMI	Aortic dissection
Refractory angina	
Thrombolytic therapy for AMI	**Relative contraindications**
PCI for AMI	Abdominal aortic aneurysm
Ischemic ventricular arrhythmias	Severe peripheral vascular disease
Weaning from cardiopulmonary bypass	
Bridge to cardiac transplantation	
High risk PCI	

Figure 5: Figure 5a depicts coronary flow autoregulation. Autoregulation maintains myocardial blood flow at a physiologically desirable range across a range of blood pressure (perfusion pressure). Autoregulation is achieved across a substantial range of arterial pressure, but cannot be maintained at very high levels or very low levels of artrial pressure. Autoregulation is affected by the coronary resistence bed which has a "set-point" in the mid-range of normal arterial pressure. To maintain myocardial perfusion as arterial pressure falls, recruitment of vasodilatory pathways leads to microvascular vasodilation, and maintains perfusion despite a lower driving pressure. Conversely, as arterial pressure rises, withdrawal of resting vasodilatory pathway activity leads to resistance vessel contraction, and avoidance of tissue hyperemia, despite elevated arterial pressure. Figure 5b demonstrates the loss of the autoregulation effect in the presence of myocardial ischemia, which leads to maximal resistance vessel vasodilation, and therefore a linear relationship of coronary flow to arterial pressure. Hence, augmentation of native pressure may lead to augmentation of flow.



rupture. Major bleeding (requiring transfusion and/or surgery) occurred in 5% and ischemia (requiring surgery or amputation) in 3%. Independent risk factors for major complications were the presence of peripheral vascular disease, female sex, and low body surface area. Other studies have additionally demonstrated diabetes and longer balloon duration to be predictors of complications.[9]

The issue of peripheral vascular disease (PVD) and IABC

The most regularly problematic context is iliofemoral artery:catheter size mismatch, and leg ischemia on that basis. Advanced PVD and small body size are problematic. As catheter/sheath designs progressively improve (made smaller), leg ischemia will likely be less of a problem, but will no doubt remain an issue in the smallest patients and in those with advanced PVD.

In some patients with an obstructed iliofemoral artery, the IAB may be surgically inserted through an abdominal approach or through a sternal approach. This is seldom performed outside of primary intention open-heart surgery as an LV assist in the immediate post-operative period. The presence of an abdominal aortic aneurysm (AAA) is not an absolute contraindication to IABC; although the risks of IABC are likely increased in this scenario. As >95% of AAAs are infrarenal, the IAB is usually above the AAA. However, dislodgement of an AAA mural thrombus during insertion, iliofemoral disease concomitant with the AAA, and concomitant advanced atheromatous disease of the thoracic aorta will increase complications of IABC in the context of AAAs.

IABC in acute myocardial infarction reperfusion therapies

The increase in diastolic pressure and coronary blood flow afforded by IABC is intuitively attractive for increasing delivery of intravenously delivered fibrinolytic agents to a coronary thrombus. The delivery of fibrinolytic agents at *normal arterial pressures* is believed to be important, as the diffusion of these very large molecules into thrombus has been well demonstrated in experimental preparations to depend on pressure-diffusion. As well, clinical trials of fibrinolytic agents, which included only small numbers of Killip Class IV patients, have failed to show evidence of benefit from administration of these agents.

Animal studies have demonstrated that reperfusion occurs up to three times faster in the presence of aortic counterpulsation, but there is no reduction in the rate of reocclusion.[7] Unfortunately, little clinical data is available in humans. Kumbasar and colleagues demonstrated increased achievement of TIMI-3 flow and a trend toward reduced mortality associated with

IABC in combination with streptokinase for acute anterior infarction, compared with streptokinase alone.[12] However, this was not randomized data. As such, the role of IABC in fibrinolytic therapy in the non-cardiogenic shock patient remains unproven.

More data are available on the role of IABC in percutaneous coronary interventions (PCI). In a randomized trial of IABC in patients with acute myocardial infarction (AMI), Ohman and colleagues showed that IABC significantly reduced both the rate of late reocclusion and the occurrence of a composite endpoint of death, myocardial infarction, or refractory ischemia.[13] The author then concluded that IABC can be combined with emergency percutaneous intervention to improve patient outcome in AMI. However, these data date back to the PCI era before stents and glycoprotein IIb/IIIa inhibitors were in widespread use. A more recent randomized trial by Van't Hof showed no improvement in survival, reinfarction or myocardial salvage associated with the use of IABC in high risk patients undergoing primary angioplasty for AMI.[14] Additionally, the PAMI-II trial also demonstrated that prophylactic IABC does not favourably alter outcome in high risk primary angioplasty.[15]

IABC in cardiogenic shock

Cardiogenic shock complicates approximately 7% of AMIs presenting to hospital. While mortality remains extremely high at approximately 70%, significant improvements have been observed in survival over the past two decades.[16] This is due in part to the increasing aggressiveness of cardiologists in pursuing early revascularization in the shock patient. IABC is also being used with increasing frequency in this patient population.

Two randomized trials from the pre-thrombolytic era showed no significant benefit from IABC in cardiogenic shock.[17,18] Unfortunately, this has not been readdressed in a randomized fashion in the new era of therapeutics for AMI. However, retrospective studies of large databases have supported the use of IABC in this setting.

The GUSTO-1 trial,[19] comparing four thrombolytic therapies in over 41,000 patients, enrolled 310 patients who were in cardiogenic shock at the time of enrollment. Anderson and colleagues compared the outcome of the 62 patients (20%) who received IABC within 24 hours of enrollment with the 248 (80%) who did not.[20] Mortality at one year was significantly lower in the group receiving early IABC, prompting the authors to suggest that IABC is underutilized in patients presenting with cardiogenic shock.

Similarly, retrospective analysis of the 856 patients in the SHOCK trial[21] registry also support the early use of IABC in cardiogenic shock. This trial randomized patients presenting to hospital with shock from left ventricular failure due to AMI to a strategy of early revascularization (within 6h of randomization) vs. medical stabilization (with any revascularization delayed at least 54 hours) and showed significant mortality benefit at 6 months in the early revascularization group. When Sanborn and colleagues compared the outcome of patients according to whether or not they were treated with IABC, they found a 31% relative risk reduction (22% absolute risk reduction) of death with IABC use.[22] However, it must be noted that IABC was utilized much more commonly in patients randomized to early revascularization. In such non-randomized data, there is significant selection bias as to which patients receive IABC, and as such, the independent value of this therapy remains unproven. However, an aggressive strategy of combining IABC with early revascularization is of proven benefit.

What about the role of IABC in the community hospital setting, where revascularization is not immediately available? Again, the lack of any randomized data confounds an evidence-based answer to this question. A single study of 335 patients retrospectively looked at the rate of community hospital survival in patients with AMI and cardiogenic shock according to whether or not they received IABC combined with thrombolytic therapy.[23] They found that a strategy of combining IABC with revascularization resulted in significantly greater survival to transfer (93% vs 37%, p=0.0002) and ultimate revascularization (85% vs. 37%).

Completing a randomized trial to prove the utility of IABC in cardiogenic shock has proven to be an insurmountable challenge thus far. TACTICS was to be a large multicentre trial enrolling patients with cardiogenic shock to thrombolysis plus IABC vs. thrombolysis alone. Unfortunately, Ohman and colleagues informed the European Society of Cardiology meeting this past August that they were able to enrol only 57 of a planned 500 patients and that the study was discontinued due to poor recruitment.[24] This is likely due both to the challenge of enrolling critically ill patients as well as to a growing sentiment among cardiologists that IABC is indicated in this setting and that withholding this therapy would be unethical.

Finally, IABC is commonly used for cardiogenic shock due to mechanical complications of AMI, such as ventricular septal rupture and acute mitral regurgitation. In this setting, the hemodynamic support of IABC serves only as a bridge to ultimate definitive surgical therapy.

Summary

Intra-aortic balloon counterpulsation favourably affects hemodynamics, myocardial performance, and

coronary blood flow. There is a significant rate of major complications associated with IABC, but the benefits outweigh these risks in a number of clinical scenarios. While there does not appear to be a role for IABC in percutaneous reperfusion interventions, its role in fibrinolytic therapy, particularly in the community setting where PCI is not available, is unclear but appears promising. This therapy is most commonly used in the setting of cardiogenic shock. While direct randomized data supporting the benefit of IABC in this setting are lacking, such a study will likely never be accomplished. The totality of the evidence available to date supports aggressive IABC use combined with early revascularization, and also suggests that this strategy is currently underutilized.

References

1. Harken DE (1958) Presentation at the International College of Cardiology, Brussels, Belgium
2. Moulopoulos SD, Topaz S, Kolff WJ. Diastolic balloon pumping (with carbon dioxide) in the aorta – a mechanical assistance to the failing circulation. *Am Heart J* 1962; 63: 669
3. Kantrowitz A, Tjonneland, S, Freed PS. Initial clinical experience with intra-aortic balloon pumping in cardiogenic shock. *JAMA* 1968; 203:135.
4. Bregman D, Casarella WJ. Percutaneous intra-aortic balloon pumping: Initial clinical experience. *Ann Thorac Surg* 1980; 29:153.
5. Zehetgruber M, Mundigler G, Christ G, et al. Relation of hemodynamic variables to augmentation of left anterior descending coronary flow by intra-aortic balloon pulsation in coronary artery disease. *Am J Cardiol* 1997; 80(7):951-955.
6. Kern MJ, Aguirre F, Bach R, Donohue T, Siegel R, Segal J. Augmentation of coronary blood flow by intra-aortic balloon pumping in patients after coronary angioplasty. *Circulation* 1993;87(2):500-511.
7. Gurbel PA, Anderson RD, MacCord CS, Scott H, Komjathy SF, Poulton J, Stafford JL, Godard J. Arterial diastolic pressure augmentation by intra-aortic balloon counterpulsation enhances the onset of coronary artery reperfusion by thrombolytic therapy. *Circulation* 1994;89(1):361-365.
8. Hutchison SJ, Thaker KB, Chandraratna PA. Effects of intra-aortic balloon counterpulsation on flow velocity in stenotic left main coronary arteries from transesophageal echocardiography. *Am J Cardiol* 1994;74(10):1063-1065.
9. Gottleib SO, Brinkler JA, Borkon AM, Kallman CH, Potter A, Gott VL. Identification of patients at high risk for complications of intra-aortic balloon counterpulsation: a multivariate risk factor analysis. *Am J Cardiol* 1984; 53: 1135-1139.
10. Gol MK, Bayazit M, Emir M, Tasdemir O, Bayazit K. Vascular complications related to percutaneous insertion of intra-aortic balloon pumps. *Ann Thorac Surg* 1994; 58:1476-1480.
11. Cohen M, Dawson MS, Kopistansky C, McBride R. Sex and other predictors of intra-aortic balloon counterpulsation-related complications: prospective study of 1119 consecutive patients. *Am Heart J* 2000;139(2):282-287.
12. Kumbasar SD, Semiz E, Sancaktar O, Yaleinkaya S, Ermis C, Deger N, .et al. Concomitant use of intra-aortic balloon counterpulsation and streptokinase in acute anterior myocardial infarction. *Angiology* 1999.50(6):465-471.
13. Ohman EM, George BS, White CH, et al. Use of aortic counterpulsation to improve sustained coronary artery patency during acute myocardial infarction: results of a randomized trial. *Circulation* 1994; 90(2):792-799.
14. 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.
15. Stone GW, Marsalese D, Brodie BR. A prospective, randomized evaluation of prophylactic intra-aortic balloon counterpulsation in high risk patients with acute myocardial infarction treated with primary angioplasty. *J Am Coll Cardiol* 1997; 29:1459-1467.
16. Goldberg RJ, Samad NA, Yarzebski J, Gurwitz J, Bigelow C, Gore JM. Temporal trends in cardiogenic shock complicating acute myocardial infarction. *NEJM* 1999;340:1162-1168.
17. O'Rourke MF, Norris RM, Campbell TJ, Chang VP, Sammel NL. Randomized controlled trial of intra-aortic balloon counterpulsation in early myocardial infarction with acute heart failure. *Am J Cardiol* 1981;47:815-820.
18. Flaherty JT, Becker LC, Weiss JL, et al. Results of a randomized prospective trial of intra-aortic balloon counterpulsation and intravenous nitroglycerin in patients with acute myocardial infarction. *J Am Coll Cardiol* 1985; 6:434-446.
19. The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *NEJM* 1993; 329:673-682.
20. Anderson RD, Ohman EM, Holmes DR, et al. Use of intra-aortic balloon counterpulsation in patients presenting with cardiogenic shock: observations from the GUSTO-1 study. *J Am Coll Cardiol* 1997; 30:708-715.
21. Hochman JS, Sleeper LA, Godfrey E, et al., for the SHOCK Trial Study Group. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. *NEJM* 1999;341: 625-634.
22. 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. *JACC* 2000; 36:1123-1129.
23. Kovack PJ, Rasak MA, Bates ER, Ohman EM, Stomel RJ. Thrombolysis plus aortic counterpulsation: improved survival in patients who present to community hospitals with cardiogenic shock. *JACC* 1997; 29(7):1454-1458.
24. XXII Congress of the European Society of Cardiology. Amsterdam, the Netherlands.

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