CHAPTER

206 Recent Developments in Intensive Cardiac Care for Acute Cardiac Disorders

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Intensive cardiac care includes a wide range of cardiac emergencies that can develop into rapidly evolving life-threatening situations requiring efficient and rapid interventions. In its original concept, the CCU was designed for arrhythmia monitoring and treatment of patients with acute coronary syndromes. In present scenario, the CCU has evolved into a critical care environment that delivers care both to patients with acute single-system cardiovascular illness and to patients with more co-morbidities and multisystem organ dysfunction.

The field of cardiac intensive care continues to advance in tandem with disorders and complexity of procedures. There have been few major developments in critical care in terms of specific new treatments and substantial evidence exist regarding the use of certain strategies, though not always guidelines based. Certain older concepts have also changed in light of new data. Here we summarize what we believe to be the most important features of progress in cardiac intensive care in recent years.

IONOTROPES

Positive inotropic drugs are typically used to stabilize patients with acute decompensated heart failure in the intensive care unit, as a bridge-to-decision or bridge to heart replacement therapy. Despite evidence that inotropic therapy may increase mortality, there are clinical settings where inotropic support may be life-saving measure, and where hypoperfusion of vital organs is obvious and the need for improved perfusion is immediate.

Initial choice of vasopressor was used to based on individualexperience and institutional bias. Dopamine, the precursor for norepinephrine, was recommended as a first line agent. However, patients in shock have a diminished response to indirect-acting agents such as dopamine, because a large component of the response to dopamine is neuronal release of norepinephrine. When endogenous norepinephrine is depleted in shock states, dopamine is unable to produce adequate response.

In patients with cardiogenic shock, norepinephrine (α1&β1-adrenergicagonist), should be preferred over dopamine as the first-line vasopressor because a subgroup analysis from a major randomized trial found that patients with cardiogenic shock who received dopamine had a higher mortality than those who received norepinephrine. In addition, dysrhythmias were more common in the dopamine group.

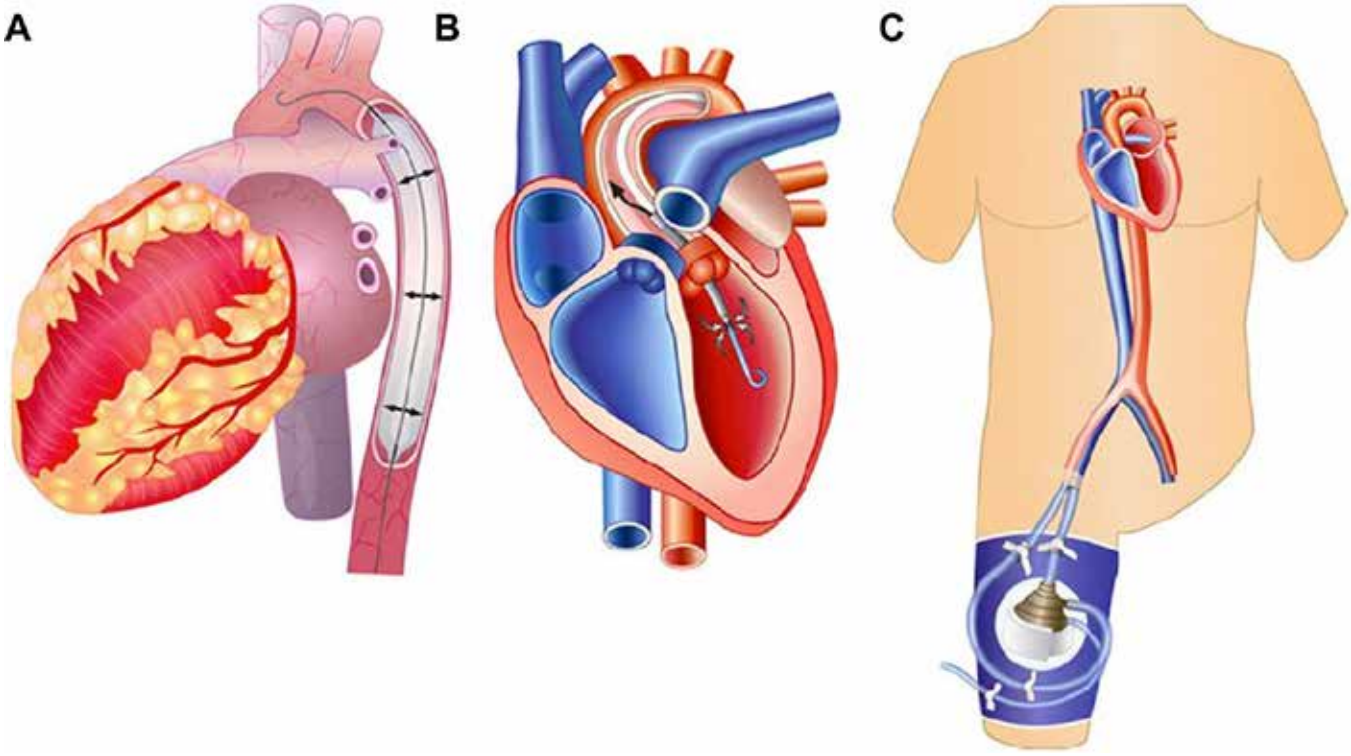

Fig. 1: An illustration of options for Mechanical Circulatory Support : (A) IABP, (B) Impella, (C) TandemHeart

Table 1: Current Guideline recommendations of IABP

Indication	ACC/AHA guidelines	ESC guidelines
STEMI with cardiogenic shock	IIa/B[a] [1]	IIb/B[a] [2]
STEMI without cardiogenic shock	-	III/A [3]
Mechanical complication of AMI	IABP can used to provide temporary circulatory support [1]	I/C [3]
High- risk PCI	IIb/C [4]	-
High-risk CABG	IIa/B [5]	

ACC, American College of Cardiology; AHA. American Heart Association; CABG, coronary artery bypass graft; ESC, European Society of Cardiology; IABP, lntra-aortic balloon pump; LVEF. left ventricular ejection fraction; PCI. percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; 1. O'Gara PT, Kushner FG, Ascheim DD, et al_ 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; 2. Steg PG, James SK. Alar D. et al. ESC guidelines for the management of acute myocardial infarction m patients presenting with ST-segment elevation Eur Heart J 2012; 33:2569-2619; 3. Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS), European Association for Percutaneous Cardiovascular Interventions. Guidelines on myocardial revascularization Eur Heart J 2010; 31: 2501-2555; 4. LevineGN. Bates ER. Blankenship JC. et al. 2011 ACCF/AHA/ SCAI Guideline for percutaneous coronary intervention A report of the Amencan College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. J Am Coll Cardiol 2011. 58:e44-el22; 5. Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA Guideline for coronary artery bypass graft surgery. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the Amencan Association for Thoracic Surgery. Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons. J Am Coll Cardiol 2011; 58:el23-e210; [a]Recently downgraded from Class I to Class II

Given concerns about increased mortality with short-term intravenous therapy with milrinone or dobutamine in patients with acute decompensated heart failure, these drugs are not to be used in the routine management of such patients. However, administration should be considered in patients with severe hemodynamic compromise with low cardiac output that is not adequately managed by diuretics and vasodilators.

Calcium sensitizing agents such as levosimendan exert positive inotropic effects on the heart by increasing the contractile apparatus sensitivity to calcium. Therefore, such drugs have the advantage of driving contractile state without increasing cAMP or calcium, both of which have adverse effects. Despite improvement in hemodynamics, there is no clear evidence of short term or long term clinical benefit. Two randomized trials with levosimendan, REVIVE-II and SURVIVE, indicated no difference in mortality with levosimendan and use was associated with more adverse effects in form of hypotension.

Newer drugs are still under intense investigation and are in clinical trials. Omecamtiv mecarbil is the first selective cardiac myosin activator and increases the efficiency of heart muscle contraction. ATOMIC AHF trial showed that the drug didn't have the usual adverse effects (e.g., tachycardia and arrhythmia) of traditional inotropic agents. Omecamtiv mecarbil may not be an inotrope, but it does improve myocardial systolic performance. Istaroxime is a novel intravenous drug that inhibits Na/ K+ ATPase and stimulates SERCA2a. HORIZON-HF study assessed the hemodynamic effects of Istaroxime and showed reduction in PCWP and increase in systolic blood pressure but no effect on neurohormones, renal function, ortroponin levels.

The quest to develop more effective and safer positive inotropic drugs is continuing. Additional targets may include improved mitochondrial function through modulation of oxidative stress iron handling, and biogenesis. Newer positive inotropic agents will also have greater advantages if they can be given orally.

CIRCUILATORY ASSIST DEVICES

Intra-Aortic Balloon Pump

Major categories of circulatory assist devices include: IABP, non-IABP percutaneous mechanical circulatory assist devices, and ECMO (Figure 1).

The intraaortic balloon pump is the device cardiologists are most familiar with and has been in clinical use for more than 4 decades, largely on the basis of favorable observational data as well as the beneficial effect on coronary blood flow, myocardial oxygen demand and hemodynamic support. It can be inserted easily and rapidly, is the least expensive of all the devices, and does not require continuous monitoring by technical support personnel.

The use of IABP during high-risk PCI, acute myocardial infarction, and cardiogenic shock had been present with the paucity of adequately powered randomized controlled trials in these settings (Table 1).

In a trial on patients with AMI and Cardiogenic Shock, in a comparison of IABP with standard therapy, no difference in 30-day mortality or in any key secondary end points (hemodynamic stabilization, length of stay in the ICU, lactate levels, dose and duration of catecholamine therapy, and RFT) was found. Although IABP was safe, there was no evidence that it wasassociated with hemodynamic improvement.

CRISP-AMI trial randomised patients with high-risk anterior STEMI without shock to a routine strategy of IABP prior to PCI lasting at least12 hours after PCI

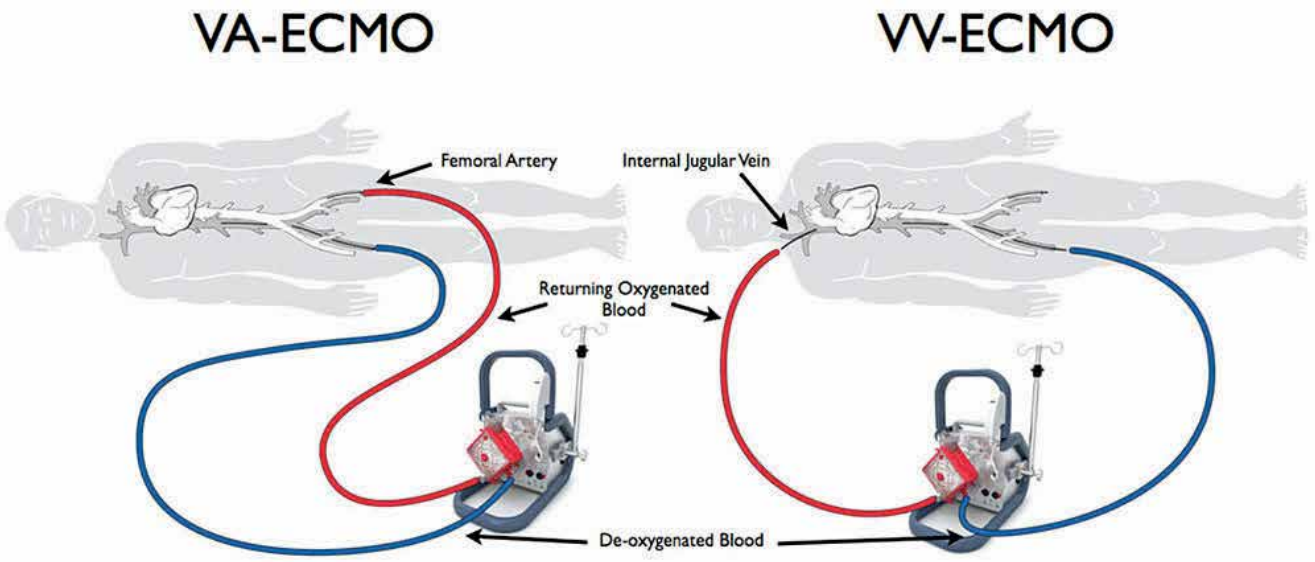

Fig. 2: Circuit configuration for VA and VV-ECMO

compared with PCI alone. This strategy did not lead to a reduction in myocardial infarct size and clinicaloutcomes at 6 months were not significantly different between the 2 groups. However, 8.5% of patients in the PCI alone group crossed over to rescue IABP therapy. These findings thus support a standbystrategy (rather than routine use) of IABP during primary PCI in high-risk anterior STEMI patients.

In patients undergoing high-risk PCI, IABP insertion was found to be effective in two observationstudies by Briguori et al. These results were not supported by the Balloon Pump Assisted Coronary Intervention Study (BCIS-1), which showed elective IABP insertion did not reduce the incidence of MACCE followingPCI and thus do not support a strategy of routine IABP placement before PCI in all patients with severe left ventricular dysfunction and extensive coronary disease. A recent meta-analysis on similar group of patients by Romeo et al., also highlighted the lack of benefit of prophylactic IABP at reducing in-hospital mortality and MACCE.

IABP is thus simplest to deploy circulatory assist device and to be used as an adjuvant treatment in presence of hemodynamic impairment. Table I shows the current recommendations.

Percutaneous Ventricular Support Devices

The limitations of IABP led to development of other percutaneous mechanical circulatory devices, in that they provide greater improvement in hemodynamic parameters. Short-term mechanical circulatory support devices are again designed to be used for a wide range of clinical conditions ranging from prophylactic insertion for high-risk PCI to management of cardiogenic shock, ADHF, or cardiopulmonary arrest.

Percutaneously inserted LVADs, such as Tandem Heart and Impella, are potential options for short-term Mechanical Circulatory Support (MCS) in the acute setting. Tandem Heart is a percutaneous left atrial to aorta assist device and Impella microaxial flow device is left ventricle to aorta assist device.

In head-to-head randomized comparison between the Tandem Heart and IABP in patients undergoing primary PCI, hemodynamics were significantly improved in the pVAD group; however, there were more complications with similar 30-day mortality rates.

Impella 2.5 have been evaluated in patients undergoing non emergent high-risk PCI in PROTECT II trial, which has shown no significant difference in the primary end point of major adverse events at 30 days between Impella 2.5 or IABP.

The EUROSHOCK Registry, a retrospective study of patients with AMI with CS undergoing implantation of Impella 2.5, showed decrease in lactate levels at 48 hours suggesting improved organ perfusion, but with high 30-day mortality at 64.2%.Patients who received Impella 2.5 support prior to primary PCI in the setting of AMI and cardiogenic shock, rather than after PCI, fared better. The Impella 2.5 has also shown beneficial LV remodeling and unloading in anterior STEMI patients without cardiogenic shock.

Multiple factors must be considered when choosing MCS including: the hemodynamic condition of the patient, hemodynamic impact of the device, technical considerations including ease and rapidity of insertion, and the ultimate goals of support.

In emergent situations, IABP is often selected as the quickest and most familiar way to obtain some degree of hemodynamic stabilization, especially in the setting of AMI with pump failure. The initial effects of the IABP on coronary blood flow may be particularly desirable in this setting as well. If hemodynamic compromise occurs despite appropriatemedicalmanagement and/or IABP, one may consider more powerful hemodynamic support devices such as an Impella.

EXTRACORPOREAL MEMBRANE OXYGENATION

Mechanical cardiopulmonary support can be delivered

in a more prolonged fashion in an intensive care unit, as extracorporeal membrane oxygenation (ECMO). There are two types of ECMO - venoarterial (VA) and venovenous (VV) (Figure 2). Both provide respiratory support like in severe ARDS with refractory hypoxemia and hypercapnia, but only VA ECMO provides hemodynamic support.

VA-ECMO can provide acute support in cardiogenic shock or cardiac arrest. The first successful use of extra-corporeal membrane oxygenation (ECMO) for treatment of cardiogenic shock was described in 1973. Observational studies and case series have reported increased survival rates among patients who received ECMO for cardiac arrest or severe cardiogenic shock as compared to conventional CPR.

In patients with acute coronary syndrome who were unresponsive to conventional CPR, ECMO plus intra-arrest PCI was associated with improved outcomes in patients who were unresponsive to conventional cardiopulmonary resuscitation.

Long-term survivors of ECMO performed for cardiogenic shock have better general health, physical health, and social functioning than patients who require chronic hemodialysis, have advanced heart failure, or have recovered from ARDS.

VA-ECMO is thus a strategy for supporting patients with cardiovascular collapse as a bridge to recovery or more definitive therapies, and provide a short-term and long-term survival advantage.

HIGH-DOSE DIURETICS VS ULTRAFILTRATION

Ultrafiltration should be reserved for patients with fluid overload who do not achieve an adequate response to an aggressive diuretic regimen (Class IIb recommendation).

Initial studies supporting use of ultrafiltration in HF were small but provided safety and efficacy data in acute HF. Ultrafiltration ascompared with diuretic therapy resulted in a higher rate of sodium and volume removal, greater weight loss and less frequent rehospitalizations and thus can provide more effective relief of congestion than pharmacologic therapy can. CARRESS-HF challenged this understanding of the effectivenessof ultrafiltration and concluded that ultrafiltration did not result in greater weight loss or improved renal function as compared with pharmacologic therapy and was associated with a similar rate of death or rehospitalization for ADHF. Thus, the use of a stepped pharmacologic-therapy algorithm was superior to a strategy of ultrafiltration for the preservation of renal function at 96 hours, with a similar amount of weight loss with the two approaches. Ultrafiltration was also associated with a higher rate of adverse events.

NON-INVASIVE VENTILATION

Noninvasive positive pressure ventilation (NPPV) refers to positive pressure ventilation delivered through a noninvasive interface. There is high quality evidence from meta-analyses and randomized trials that NPPV decreases the need for intubation, hospital mortality and improves respiratory parameters (eg, heart rate, dyspnea, hypercapnia, acidosis) in patients with cardiogenic pulmonary edema.

However, Three Interventionsin Cardiogenic Pulmonary Oedema study (3CPO), compared modes of ventilation with standard therapy and each other, detected no differences in mortality or need for intubation, in contrast to most preceding studies (although it did find more rapid improvements in patient-reported dyspnea, acidosis, and hypercapnia).The limitation was that they excluded sick patients who required life-saving or emergency intervention, a population that is more likely to benefit from NIV.

Sleep-disordered breathing is common in patients who have heart failure with reduced ejection fraction, with prevalence of 50-75%. Adaptive servo-ventilation is a noninvasive ventilatory therapy that alleviates central sleep apnea by delivering servo-controlled inspiratory pressure support on top of expiratory positive airway pressure. In the SERVE-HF trial, however, there was no significant effect of adaptive servo-ventilation on the primary composite end point in the time-to-event analysis of the first event of death from any cause, lifesaving cardiovascular intervention, or unplanned hospitalization for worsening heart failure. Unexpectedly, there was higher all-cause and cardiovascular mortality in the adaptive servo-ventilation group than in the control group.

However, no safety concerns have been identified during the short term application of positive airway pressure in patients with decompensated heart failure and thus non-invasive ventilation is considered as adjunctive therapy in patients with acute cardiogenic pulmonary edema who have severe respiratory distress or whose condition does not improve with pharmacologic therapy.

CONCLUSION

The field of critical care cardiology has undoubtedly grown over the past several years. Patients in cardiogenic shock represent an extremely high risk group in whom mortality has remained high despite revascularization and pharmacologic therapies. Stabilization therapy often begins with intravenous inotropic agents. In the setting of profound cardiogenic shock, IABP is less likely to provide benefit than continuous flow pumps including the Impella and Tandem Heart. ECMO may also provide benefit, particularly for patients with associated impaired respiratory gas exchange and patients unresponsive to conventional CPR. Application of high quality, appropriate, evidence-based medicine to these complex, high-risk cardiac patients requires formal training in this field.

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