Aspects of Percutaneous Cellular Cardiomyoplasty

Matthew Hook, MD and Patrick Whitlow, MD

SUMMARY

The significant advances achieved over the past decade in the field of percutaneous coronary intervention have significantly increased our ability to use catheter-based techniques to modify cardiac physiology. The ongoing studies demonstrating the significant potential of cell-based therapy for the prevention and treatment of chronic heart failure has led to the development of multiple catheter-based systems for the delivery of cells to the injured myocardium. Advances have also been made in catheter-based systems that exploit electromechanical properties of the heart in order to direct the interventionalist as to the best areas in which to inject cells. In this chapter we will review the different catheter systems currently available or under development as well as discuss how different features of each may be optimal in the different settings of acute myocardial infarction and chronic heart failure.

Key Words: Intracoronary delivery; endocardial injection; electromechanical mapping; ischemic cardiomyopathy.

Percutaneous catheter-directed regenerative cell therapies are being developed for patients with compromised systolic function and prior myocardial infarction (MI), ischemic and nonischemic cardiomyopathy, as well as for patients with acute myocardial injury, presenting for revascularization (1–3). The administration of skeletal myoblasts at the time of acute revascularization for MI is intriguing, as patients may benefit from increased adaptability of the cells in a milieu of intense recruitment of native progenitor cells and better blood supply than those with chronic myocardial scar tissue (4,5).

Some progenitor cells and skeletal myoblasts do not home from the blood stream into the myocardium, and thus, direct delivery of these cells into infarct or peri-infarct beds of myocardium may be required. Although both surgical and percutaneous approaches have been developed and tested in preclinical and clinical studies, a percutaneously based mode of delivery is desirable for several reasons:

1. It helps to avoid an open surgical procedure and the concomitant risks of infection, bleeding, general anesthesia, etc.
2. Surgical/epicardial approaches fail to access the interventricular septum, vital for synchronization of myocardial contraction, while constituting a moderate percentage of ventricular mass.
3. Percutaneous-based therapies are less invasive in the event of the need for recurrent myocardial injections.
4. If cells need to be delivered at the time of revascularization from an acute MI, it is unlikely that a surgical approach will be readily accessible.

PERCUTANEOUS CELL THERAPY FOR ACUTE MI

If cell delivery is to be undertaken at the time of coronary reperfusion, it implies that an allogeneic cell that is available at the time of patient presentation has been developed. Like a cell that is available at all times, the procedure to deliver them also needs to be available at all times as well. Therefore, the delivery strategy needs to take into account the fact that patients will present at all hours of the day and night. Ideally, patients with an acute MI receiving cell therapy at the time of primary revascularization would do so via a perfusion catheter or an over-the-wire balloon in the infarct-related artery. Concerns regarding this technique relate primarily to ascertaining allogeneic progenitor cells for patients presenting acutely, the adverse effects of cellular embolization in an acutely occluded vessel, as well as a potential for increased rates of in-stent restenosis in target vessels treated with bare-metal stents (6). Delivery via the infarct-related artery would theoretically eliminate the need for electromechanical mapping or other imaging techniques that could prove cumbersome at the time of primary percutaneous coronary intervention (PCI).

Intracoronary injection of cells has recently been proven safe and moderately effective in a small randomized trial of patients with chronic myocardial injury and in the Myoblast Autologous Grafting in Ischemic Cardiomyopathy cell trial, in which patients were randomized only if they presented more than 48 hours after symptom onset and were hemodynamically stable for more than 24 hours prior to randomization (6,7). No trial has yet to address the safety or efficacy of infusing stem cells at the time of revascularization in patients presenting for primary percutaneous revascularization.

CELL THERAPY FOR CHRONIC HEART FAILURE

An ideal route of delivery would be minimally invasive and would send high concentrations of stem cells to a target region of an organ, while avoiding inundating other organs. Direct intramyocardial delivery during surgery and percutaneous delivery via the coronary, arterial-transendocardial, or venous-transendocardial routes is being used or proposed in clinical trials. Intracoronary or intravenous delivery to access a specific region close to the coronary vasculature is effective and is easier to perform than direct injection.

Many have proposed that intramyocardial delivery from the endocardium requires an imaging modality that can discern healthy from injured or dead tissue (8–10). In one study, electromechanical mapping was used to identify viable myocardium for catheter-based transendocardial delivery of mononuclear bone marrow cells in humans using the NOGA system (Cordis) (11). This electromagnetic tracking system used an injection catheter to differentiate and map normal, scarred, and viable myocardial tissue (8). During a standard clinical procedure using the NOGA, three external magnets that emit a low-energy magnetic field are placed at different locations around the patient’s chest. The system uses a catheter equipped with three sensing coils and two electrodes on its distal tip that permit measurement of a voltage potential across a short segment of endocardium (11). The coordinates of the catheter tip in three-dimensional space are