Selection of best door-to-cardiac regeneration (D2CR) time

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Short Communication

Abstract

In spite of great progress in the treatment of acute coronary syndrome (ACS) events in reperfusion era, patients are still at risk for development of heart failure due to negative remodeling. Thus, the importance of regenerative therapies in parallel with reperfusion strategies is fundamental. A key feature in this case is obtaining the most appropriate door-to-cardiac regeneration (D2CR) time. This golden time in which fresh stem cells can invade scare-prone tissue could be defined as door-to-cardiac stem cell (D2CSC) plus door-to-cardiac regeneration (D2CR) time. Application of stem cells in this golden time allows comprehensive regeneration and reconstruction. Therefore, the aim of this study was to plan the outlines of simultaneous application of cellular and vascular reconstruction strategies.

Keywords: Cardiac Regeneration, Stem Cell, Golden Time

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Introduction

Despite the huge progress made in the treatment of patients suffering from acute coronary syndrome (ACS) in reperfusion era, patients are still at high risk for development of heart failure due to the progressive negative remodeling: "myodegeneratio cordis".[1] Thus, adjunct therapies should run with a pace similar to the advanced reperfusion strategies. In this case, earlier stem cell therapies at stages before the need for regenerative therapies have been paid more attention in recent decades. Stem cell therapy in ACS is still in its infancy and more light must be shed on this state-of-science field.

By improvement of health care systems, the goal of ACS care must change from prompt cell survival to restoration of wild type cardiac cells, a battle against initiation of negative remodeling. The goal is prevention from progression to heart failure, which is a growing epidemic in this age. Indeed, appropriate cell therapy results in prolonged enhanced mobilization of endogenous reparative stem cells from bone marrow.[2] What needs to be known is the best time cells can be applied after ACS. Appropriate door-to-cardiac regeneration (D2CR) time should be defined as the golden time which fresh stem cells can invade scar-prone breath lost tissue and facilitate cardiomyocyte survival by escaping from post-infarct cardiosclerosis. It might not be the same as door-to-balloon (D2B) or door-to-needle (D2N) time, since the goals are not truly the same. The former aims to restore functionally and anatomically dead cardiomyocytes, but the latter seeks prompt reperfusion and prohibition of ongoing cell death. This time might actually be divided into temporal intervals as adjunctive to early or late reperfusion strategies. Since activation, mobilization, homing, differentiation, and integration of endogenous and resident cardiac stem cells are additive approaches for cardiac repair, D2CR time includes subdivisions of door-to-cardiac stem cells (D2CSC) or door-to-recruit endogenous progenitor cells (D2REPC). However, total door-to-cardiomyoplasty (D2C) time contains door-to-reperfusion time (D2N+D2B times) plus D2CR time (Figure 1). This is the golden time during which reconstruction should be established for comprehensive regeneration (vascular, muscular, electrical, metabolic, and genomic). The exact time is still inconspicuous, but obviously it cannot be defined in its net number as reperfusion strategies and the goals should be understood as the longest time interval that can be considered acceptable for a system. It refers to the diversity of stem cells and their natural cell cycle. As an example, based on the available data of bone-marrow derived mononuclear cells it is 17.5 ± 0.8 d for trans-epicardial and 7 days for trans-coronary delivery rout.[3,4] This time is reported to be 10-14 hrs for intra-coronary application of bone-marrow derived CD133 cells.[5]

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Discussion

Evidently, not all patients are candidate for reception of such cardiomyocyte accretion procedures. Patients suffering from ACS with lower baseline ejection fraction or no-option ACS cases with markers of infarct expansion and poor rehabilitation seem to be benefited more from "cellular bypass". Individually, adjunctive, facilitated, or rescue cellular interventions might be the only possible care for 5-10% of ACS cases. Strictly speaking, to define this time for indicated cases various options should be abstracted into principal instructive keys as the time for preparation and delivery of chosen cells, and the time for delivered cells to get committed for appropriate actions in cardiac milieu. The former depends on the applied cell characteristics in terms of cell type, dosage, and its bio-distribution properties. The latter, depends on the cell delivery technique, the location of cell delivery, and cell trans-differentiation. Often, a lag phase after ACS allows better cell compliance. In these circumstances, the time is obligatory immediately after harnessed inflammatory flood of plaque rupture/erosion and before initiation of scar expansion. Ultimately, these factors are totally inter-related as a chain. Clearly, the individualized application of appropriate stem cell which seeks its own administration method is the principal part of the therapeutic cascade. As an example, for scar strengthening purposes, direct injection of myoblasts or pre-programmed adult stem cells meets the needs rather than mesenchymal stem cells. Selection of eligible cells to combat the hostile milieu of cardiac tissue after ACS is just one side of the coin, but it is not within the scope of this article. Cellular cardiomyoplasty is a gradually growing field. Menasché et al. opened new horizons to cardiac therapeutics by performing the world's first clinical cellular neomyocardial formation and revitalization of scar tissue.[6] I tried to scheme the dream of simultaneous application of cellular and vascular reconstruction strategies. The idea of pre-occurrence cell reservation banks seems to be developed to bypass cell cultivation and processing time. By a small biopsy taken from vastus laterialis or even usage of other cell resources, like adipose tissue-derived stem cells or umbilical cords at the time of birth, each person can have reserved his or her own cell ready to use. Finally, the best applied time is the time during which cell application is able to thicken infarct walls and prohibit deterioration of ejection fraction and negative remodeling.

Conflict of Interests

Authors have no conflict of interests.

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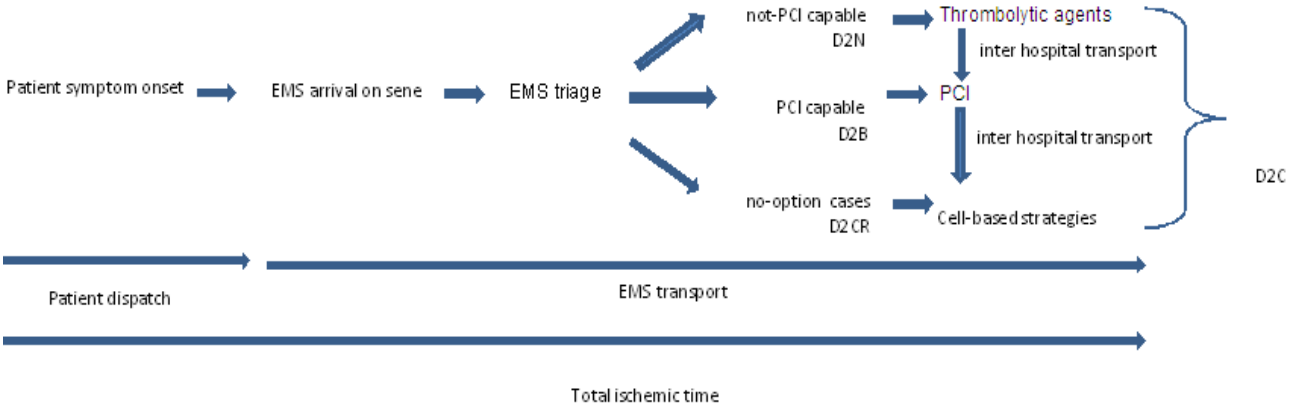

Figure 1. Options for transporting acute coronary syndrome (ACS) cases and recommended strategies for ideal cardiomyoplasty
EMS: Emergency medical services; PCI: Percutaneous coronary intervention
D2B: Door-to-balloon; D2N: Door-to-needle; D2CR: Door-to-cardiac regeneration; D2C: Door-to-cardiomyoplasty

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