Retention of mesenchymal stem cells in the heart is lower after retrograde coronary venous infusion compared to intracoronary infusion in a porcine model of chronic myocardial infarction

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Background: An important aspect of cell therapy in the field of cardiac disease is safe and effective delivery of cells. Commonly used delivery strategies such as intramyocardial injection and intracoronary (IC) infusion both present with advantages and disadvantages. Therefore, alternative delivery routes are explored, such as retrograde coronary venous infusion (RCVI).

Purpose: The aim of this study is to compare cardiac cell retention between RCVI and IC infusion. The secondary endpoint is safety of RCVI.

Methods: Myocardial infarction (90 minutes LAD occlusion) was induced in 16 female, landrace pigs. Four weeks later, the surviving 12 pigs were randomized to receive a median of 3.1 million [interquartile range 2.6 – 3.5] bone marrow-derived porcine mesenchymal stem cells (MSCs) in 10 ml phosphate buffered saline, labeled with the radioactive isotope Indium-111 either via RCVI (n=6) or IC infusion (n=6). In case of RCVI, 40ml of sodium chloride was infused on top of the 10ml of cell suspension in order to fill the coronary venous system and prevent cells from only staying in the coronary sinus. Four hours after cell administration, nuclear imaging was performed to determine the amount of cells retained in the heart as a percentage of cells retained in the whole body of the pig.

Results: A significantly lower percentage of MSCs is retained in the heart after RCVI compared to IC infusion (RCVI: median 2.89% [interquartile range 2.14 – 3.86] vs IC infusion: median 13.74% [interquartile range 10.20 – 15.41]) as presented in figure 1. Retention of cells in other organs did not significantly differ between RCVI and IC infusion, although a numeric difference in retention was seen in the lungs (RCVI: median 35.45% [interquartile range 26.53 – 45.22] vs IC infusion: median 22.07% [interquartile range 20.36 – 29.22]). RCVI led to development of pericardial fluid and hematomas on the frontal wall of the heart in three cases. Dissection of the coronary venous system after RCVI was seen in three pigs. IC infusion led to no-flow in one pig.

Conclusion: RCVI is significantly less efficient in delivering bone marrow-derived MSCs to the heart compared to IC infusion. RCVI led to more safety issues than IC infusion in this study, with multiple cases of venous dissection and development of hematomas and pericardial fluid collections.
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