CASE ANECDOTES, COMMENTS AND OPINIONS

Intraoperative processing and epicardial transplantation of autologous atrial tissue for cardiac repair

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We present the production and clinical application of autologous atrial micrografts during coronary artery bypass grafting (CABG). Micrografts are isolated from otherwise discarded atrial appendage (AA) tissue and are combined with fibrin gel

and a decellularized small intestinal submucosa (SIS) matrix sheet (Figure 1a). The technique—mechanical tissue processing, preparation of the transplant, and its topical application with a matrix sheet—is performed during CABG (Figure 1a, b). The protocol is provided in Appendix 1 (available online at www.jhltonline.org).

The transplant production takes approximately 30 minutes, whereas the isolation of the micrografts takes approximately 8 minutes for an average size tissue piece. In the production, the average weight of AA tissue was 0.895 ± 0.45 g (n = 15). Mechanical isolation yields cells and micrografts, cellular aggregates attached to their matrix (Appendix 2A-D and Movie Appendix 2, online). Cell yield was 9.76 × 10⁶ ± 0.53/g of tissue (n = 11), and cellular viability was 90.6% (n = 7). After isolation, micrografts are spread onto the SIS sheet. A slowly gelling matrix of fibrin diluted with cardioplegia is laid over the micrografts. The graft is kept metabolically inhibited on a cooling plate until transplantation.

A 64-year-old man diagnosed with coronary artery disease and heart failure was scheduled for elective bypass grafting. He had exercise dyspnea, and his angiogram showed 3-vessel disease. Our clinical safety and feasibility study (ClinicalTrials.gov identifier NCT02672163) enrolled the patient after assessing the patient’s eligibility and receiving his written informed consent.

In the beginning of the operation, a small piece of right atrial appendage was excised while the right atrium was being cannulated (Figure 1b, panels C–D) and was used for preparation of the micrografts. After the 3 bypass anastomoses were completed, but before reperfusion, the micrograft transplant was placed on the anterior wall of the left ventricle (Figure 1b, panel F) on the scar area identified in the preoperative magnetic resonance imaging. The sheet was sutured to the myocardial surface with minimal disturbance to the contracting muscle (Figure 1b, panels F-G).

The patient recovered well from the operation and was discharged from the hospital after 7 days. At the 3-month postoperative follow-up, the patient was practicing regular exercise and had returned to work. Magnetic resonance imaging at 6 months showed markedly improved movement (Movies A and B, online) and ventricular wall thickening (Figure 2) in the treated infarcted scar area.

The use of AA as the cell source provides advantages over conventional cell therapy procedures. Firstly, cells in the micrografts stay attached to their tissue-specific extra- and intracellular matrix. Secondly, cardiac tissue–derived cell population heterogeneity can serve as the basis for cardiac tissue arrangement and give rise to an array of paracrine signals. The progenitor and stem cell pools in the AA help drive neovascularization and myocardial tissue-type differentiation directly or via paracrine effects.

The AA-derived micrografts can be further modified by or supplemented with, for example, additional matrix components, paracrine factors, microRNAs, microvesicles or microparticles, or drugs. The micrografts can also be used as vehicles for gene therapy. Taken together, the AA micrograft transplant holds great potential to serve as the future first-line cardiac cellular therapy.

Disclosure statement

None of the authors has a financial relationship with a commercial entity that has an interest in the subject of the presented manuscript or other conflicts of interest to disclose.

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1AADC Consortium members are listed in Supplementary material, available online.

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Figure 1  (a) Cardiac micrograft production in conjunction with bypass surgery. The atrial appendage is processed into micrografts, combined with fibrin and extracellular matrix sheet, and the graft is transplanted epicardially on the injured myocardium. (b) Single operation atrial appendage micrograft therapy. (A) The instrument table setup for cell transplant production with (B) the bypass operation. When the patient is prepared for on-pump surgery by cannulating the right atrium, (C) the atrial appendage (black arrow) is first occluded with a clamp and sutures, after which (D) a piece of atrial appendage tissue (black arrow) is cut and (E) collected for cell-micrograft isolation and composition of the graft. (F and G) After revascularization therapy is finished, the graft (white arrow) is transplanted epicardially. All persons appearing in the figures provided their written permissions for publication of their photographs.
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Appendix A. Supporting information

Supplementary data are available in the online version of this article at www.jhltonline.org.

References


