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Esophageal transplantation in the rat☆,☆☆,★

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Abstract

Purpose: Esophageal replacement surgery has been used to treat long-gap esophageal atresia, caustic esophageal stricture, and esophageal avulsion. Here, we report total esophageal transplantation in rats without vascular anastomosis as an option for esophageal replacement surgery.

Methods: Fourteen total segments of esophageal transplants were harvested from 24-week-old male Sprague–Dawley rats using a harvesting procedure. The segments were transplanted through the mediastinum in the esophageal bed of 15-week-old male Sprague–Dawley rats without adjacent vascular anastomosis using the transhiatal pull-up technique. The ends of the transplanted esophagus were ostomized using cervical and abdominal esophagostomies. An immunosuppressive-treated (IT) group (n = 7) received cyclosporine and cotrimoxazole for 10 days, while an untreated (UT) group (n = 7) received only cotrimoxazole for 10 days. On post-operative day 10, the rats were sacrificed, and the transplant and recipient esophagi were evaluated macroscopically and histopathologically.

Results: All transplantations were successful and all transplanted rats survived. Upon macroscopic evaluation, no evidence of complications was observed and all transplanted esophagi in the two groups appeared to exhibit excellent firm tissue; however, mild necrosis was observed in the cervical end of the transplant in one rat in the IT group. Histopathologic examination showed a viable esophageal structure in all rats. Inflammation and muscular atrophy were lower in the IT group than in the UT group, whereas vascularity was higher in the IT group than in the UT group.

Conclusion: Total esophageal transplantation was performed directly without vascular anastomosis into recipients in a rat model. This procedure should be done in larger animal models before being attempted in humans.

Esophageal replacement surgery has been used to treat long-gap esophageal atresia, caustic esophageal stricture, esophageal avulsion, and esophageal cancer using digestive organs such as the colon, stomach, ileum, or jejunum. However, esophageal replacement surgery still presents a major challenge and is associated with complications, mortality, and significant morbidity [1–4]. Experimental esophagus tissue engineering and esophageal transplantation studies are promising for this type of surgery [5–7].

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Here, we report total esophageal transplantation in rats without vascular anastomosis as an option for esophageal replacement surgery.

1. Methods

Twenty-eight adult male Sprague–Dawley rats (24-week-old rats weighing 285–325 g as donors [n = 14] and 15-week-old rats weighing 185–230 g as recipients [n = 14]) were used in the present study. All of the experimental protocols were reviewed and approved by the Institutional Animal Care and Use Committee of Dicle University (approval no. 2012/32).

The rats were fasted overnight before the experiments, but were given free access to water. Animals were anesthetized by intraperitoneal injection of ketamine (Ketalar Flakon; Pfizer, Istanbul, Turkey) at a dose of 75 mg/kg body weight and xylazine (Rompun; Bayer, Istanbul, Turkey) at a dose of 10 mg/kg body weight.

Fourteen total segments of esophagus were harvested as transplants from 14 donor rats by applying the harvesting procedure described below (Fig. 1A and B) [8,9].

After anesthesia, mid-line laparotomy was performed. First, the abdominal aorta and inferior vena cava were cannulated using a catheter (20-gauge peripheral venous cannula; B-Cat IV Cannula; Bicakcilar, Istanbul, Turkey). The entire body was washed out with 150 ml of cold (4°C) lactated Ringer's solution (Eczacibasi Baxter, Istanbul, Turkey) supplemented with 50 IU/ml heparin (Nevparin Flakon; Mustafa Nevzat, Istanbul, Turkey) via an arterial cannula. Blood was withdrawn simultaneously via a venous cannula until the withdrawn blood was watery and the liver and lungs were blanched at flushing. The total esophagus with all segments was removed from the animal, washed, and then placed in cold lactated Ringer's solution (Eczacibasi Baxter).

Fourteen total segments of harvested esophagus were transplanted through the mediastinum into the esophageal bed of 15-week-old male Sprague–Dawley rats without vascular anastomosis using the transhiatal pull-up technique described below (Fig. 1C).

After mid-line laparotomy, the stomach and distal esophagus were gently retracted. The esophageal hiatus was observed, and then a malleable probe with a blunt tip (Myrtle Leaf Probe, Product no. 09.08.20, Medicon eG, Tuttlingen, Germany) was inserted gently from the hiatus. The probe was advanced through the mediastinum blindly but gently without excessive force to the cervical area. The probe head was extracted from the right cervical area using a small skin incision. A 3-0 silk suture (Ethicon Inc., Somerville, NJ, USA) loop was interlocked with the probe head using a simple loop noose. The probe with the suture was then withdrawn and removed from the esophageal hiatus. The loop suture was untied from the probe and interlocked with the proximal end

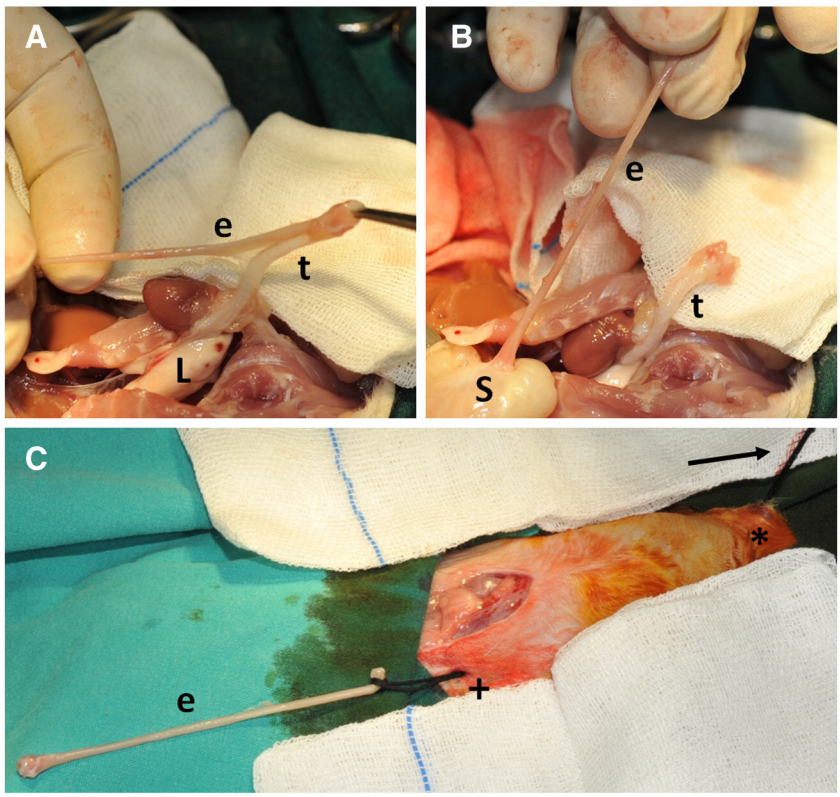

Fig. 1 A and B, Harvesting procedure. C, Transplantation procedure using the transhiatal pull-up technique (e, esophagus; L, lung; t, trachea; S, stomach; arrow, suture into mediastinum; plus sign, abdominal; asterisk, cervical esophagostomy site).