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ORIGINAL ARTICLE

Dilated ureter for esophageal substitution: A preliminary experimental study in the rat

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Summary
Background: Esophageal replacement using digestive organs such as the colon, stomach, or jejunum has been used to treat long-gap esophageal atresia and caustic esophageal strictures. Nevertheless, it presents a major challenge. Here, we report a preliminary experimental study that examined the use of a free dilated ureter as an option for esophageal substitution in a transplantation rat model.
Methods: Ten 28-week-old male donor rats underwent distal ureteral ligation for 4 weeks, and the total dilated ureters were recovered. In each of the ten recipient 20-week-old male rats, a ureter was transplanted through the mediastinum into the esophageal bed, without vascular anastomosis. All rats received cyclosporine and cotrimoxazole for 10 days. On postoperative day 10, the rats were sacrificed, and the transplanted ureters were evaluated macroscopically and histopathologically.
Results: All procedures were achieved. In the early postoperative period, three transplanted rats died. Upon macroscopic evaluation, no evidence of complications was observed, and all transplanted ureters exhibited apparently good firm tissue. Histopathological examination showed a viable ureteral structure with good vascularity, low inflammation, and regenerated epithelium in all rats.
Conclusion: As an option for esophageal substitution, heterotopic ureteral transplantation can be performed directly into the mediastinal location of the esophagus, without vascular anastomosis in a rat model. In the future, free dilated ureters might be useful for esophageal grafting or patching in humans; however, this procedure must be validated in additional large animal models before being attempted in humans.

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Introduction

Esophageal replacement (ER) using digestive organs such as the colon, stomach, ileum, or jejunum has been performed to treat caustic esophageal strictures and long-gap esophageal atresia. The preferred organ for ER is the colon with a vascular pedicle. Nevertheless, it presents a major challenge for surgeons and is associated with severe complications due to vascular events, such as necrosis, anastomotic leakage, and stricture [1—3]. Alternative non-digestive tissues such as the skin, pleura, muscle, pericardium, or fascia have failed, and tissue engineering and esophageal transplantation studies have not yet attained reliable outcomes [4—7].

Here, we report a preliminary experimental study that examined the use of a free dilated ureter as an option for ER in a transplantation rat model.

Material and methods

Twenty Sprague-Dawley rats (ten 28-week-old male rats weighing 330—345 g as donors and ten 20-week-old male rats weighing 165—180 g as recipients) 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. 2012/40).

The rats were fasted overnight before the experiments, but were given free access to water. The 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.

The ureters of the ten donor rats were dilated by applying complete unilateral ligation of the distal ureter as previously described in a hydroureter rat model, and the ureters were recovered as ER organ transplants, using the procedure described below (Fig. 1) [8—10].

After anesthesia, a midline laparotomy was performed. The ureter was identified and ligated at the location nearest the bladder with a 5-0 silk suture (Dogsan AS, Trabzon, Turkey). The abdomen was continuously closed using 2-0 silk suture material (Dogsan AS). The animals were allowed food and water immediately after the operation and during recovery from anesthesia. After 4 weeks, a midline laparotomy was again performed (Fig. 1A and B), and 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 of heparin (Nevparin Flakon; Mustafa Nevzat, Istanbul, Turkey) via an arterial cannula. Blood was withdrawn simultaneously via a venous cannula

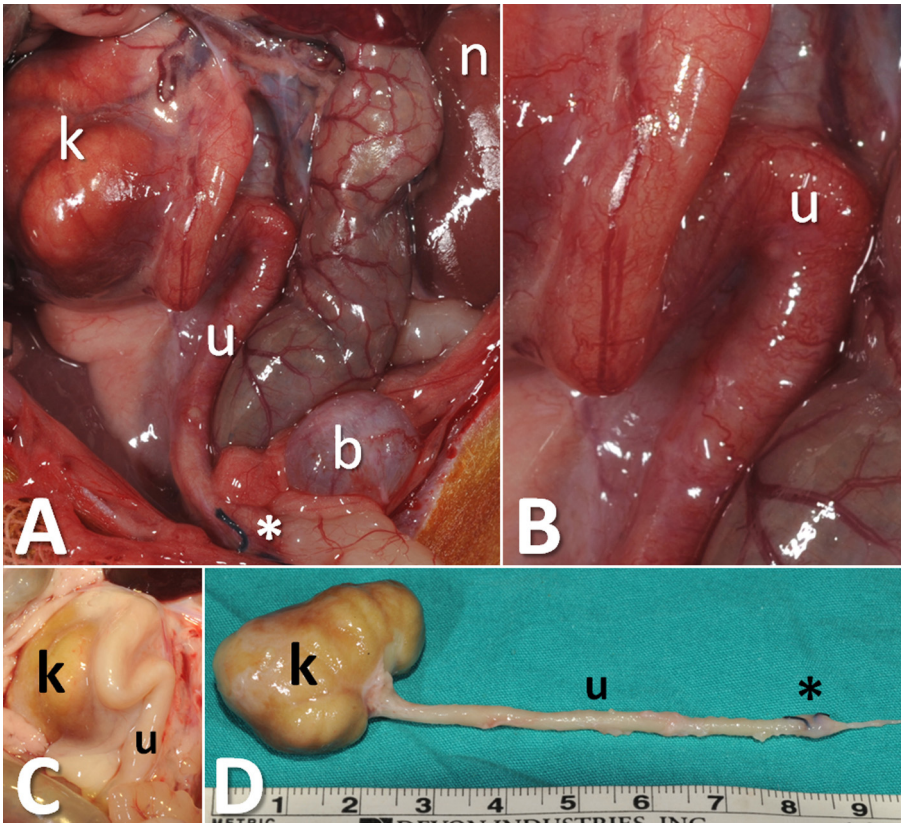

Figure 1 Recovering of the dilated ureter at 4 weeks after ligation (asterisk). Macroscopic appearance of the tortuous dilated ureter (u) with a hydronephrotic kidney (k) before (A and B) and after (C) wash-out of the total body and after recovering (D) (n: normal contralateral kidney; b: bladder).