Biodegradable vs Nonbiodegradable Cardiac Support Device for Treating Ischemic Cardiomyopathy in a Canine Heart

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Clinical studies of the efficacy of the nonbiodegradable CorCap device have shown inconsistent findings, at least in part, because of device-related impairment of diastolic cardiac function. We hypothesized that use of biodegradable material for the cardiac support device could contribute to an improvement in the diastolic function of the failing heart. Polyglycolic acid and polyethylene terephthalate were used to prepare biodegradable and nonbiodegradable cardiac support devices, respectively. Twelve-month-old beagles underwent anterior coronary artery ligation. One week after, the beagles were randomly assigned for implantation of a biodegradable cardiac support device (n = 7), nonbiodegradable cardiac support device (n = 8), or sham operation (n = 8). Twelve weeks after coronary artery ligation, the biodegradable group showed a significantly greater recovery of echocardiographical ejection fraction than the nonbiodegradable and the sham groups (40% ± 3.3%, 32% ± 2.5%, and 29 ± 2.6%, respectively). Of note, diastolic function, as assessed by Tau, –dp/dt min, and end-diastolic pressure-volume relationship in the cardiac catheter, was significantly better in both left and right ventricles in the biodegradable group than in the nonbiodegradable group. Moreover, global end-systolic wall stress was significantly lower in the 2 device groups than in the sham group ($P < 0.03$). Furthermore, global end-diastolic wall stress was significantly less in the biodegradable device group than in the nonbiodegradable group ($P < 0.02$). The cardiac support devices made of biodegradable material were more effective in improving systolic function, with preservation of diastolic function in the canine infarct heart, than devices made of nonbiodegradable material.

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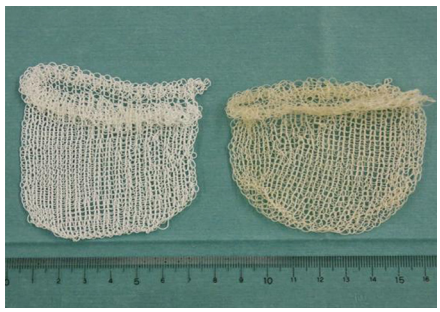

The nonbiodegradable (left) and the biodegradable (right) cardiac support devices.

Central Message

Biodegradable cardiac support devices improve systolic function in the canine infarct heart while preserving diastolic function.

Perspective Statement

Cardiac support devices reduce diastolic wall stress, preventing progressive ventricular remodeling. However, such devices may affect diastolic cardiac function. Devices made of biodegradable material are more effective than nonbiodegradable materials in improving systolic function in the canine heart, with preservation of diastolic function, and could offer a superior therapeutic alternative.

INTRODUCTION

Left ventricular (LV) remodeling in myocardial infarction (MI) involves progressive dilatation of the LV cavity and an increase in LV wall stress, leading to congestive heart failure.[1,2] The ventricular constraint procedure is a non-transplant surgical treatment for heart failure, where the entire epicardial surface is wrapped with a prosthetic material designed as a mesh support sock that is fitted around the heart. This procedure has been shown to mechanically

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reduce ventricular wall stress and prevent the progression of LV dilatation in preclinical studies involving large animal models.[3-7] Clinical studies of the CorCap device have reported its beneficial effects on LV remodeling, including a significant reduction in LV volume and a significant improvement in New York Heart Association functional class; however, no overall survival benefit was found.[7,8] These inconsistent results can partly be explained by the nonbiodegradable material used to wrap the ventricle, which can cause a chronic foreign-body response, potentially leading to epicardial constraint that impairs the diastolic function of the LV and the right ventricle (RV).

In contrast, in our group, we placed a device made from a biodegradable polyglycolic acid over the entire LV and RV in a canine model of chronic MI and found that this biodegradable material did not induce LV diastolic dysfunction associated with rigid fibrous tissue formation around the device. However, the functional effects of the biodegradable device were not directly compared with those of nonbiodegradable device implantation.[9] In the present study, we tested our hypothesis that the use of biodegradable material for the ventricular constraint procedure would contribute to greater functional benefits, diastolic function in particular, in chronic MI, compared with devices made from nonbiodegradable material.

METHODS

In this study, animal care complied with the Guide for the Care and Use of Laboratory Animals (National Institutes of Health Publication No. 85-23, revised 1996). The experimental protocols were approved by the Ethics Review Committee for Animal Experimentation of Osaka University Graduate School of Medicine.

Anesthesia and Analgesia for Animals

Twenty-three beagles (Oriental Yeast Co, Ltd) weighing 9-11 kg were used in this study. General anesthesia was induced by intramuscular injection of ketamine (10 mg/kg) and xylazine (1 mg/kg), followed by endotracheal intubation; anesthesia was maintained by intravenous propofol (2 mg/kg) and inhaled sevoflurane (1%-2%). Meloxicam (0.2 mg/kg) and cefazolin (30 mg/kg) were administered intramuscularly twice a day for 4 days, starting 1 day before the procedure. After completion of the experiments, the animals were humanely killed under general anesthesia, using an administration of intravenous potassium-based solution.[9]

Myocardial Infarction Induction

Under general anesthesia and electrocardiographic monitoring, intravenous lidocaine (10 mg/kg) was administered to prevent arrhythmias. A minimal left thoracotomy was performed through the fifth intercostal space, and the heart was exposed by pericardiotomy. The left anterior descending artery and the first and second diagonal coronary arteries were permanently ligated, both proximally and distally, using 5-0 polypropylene sutures to produce an anterior MI. After the layered closure, the animals were allowed to recover in individual temperature-controlled cages.

Design of the Cardiac Support Device

The cardiac support devices (0.9-1.1 g) were designed to cover the entire ventricular myocardium and secure to the atrioventricular groove of the chronic MI canine heart, on the basis of data obtained from multidetector computed tomography (MDCT). A 3-dimensional model was constructed, based on data derived from the contours of the heart images, and a knitting machine then used the data to create a cardiac support device. The cardiac support device was knitted fabric made from 3-0 suture. The biodegradable and nonbiodegradable cardiac support devices were made from commercially available polyglycolic acid and polyethylene terephthalate suture, respectively (Nipro Corporation; Fig. 1A). Polyglycolic acid suture has a peak tensile strength of 19.4 ± 2.1 newton (N), whereas polyethylene terephthalate suture has a peak tensile strength of 11.3 ± 1.5 N. In a rodent model, it was found that the strength of the polyglycolic acid suture in vivo halved at 2 weeks and was lost at 4 weeks, and the sutures were completely absorbed at 6 weeks.[10,11]

Treatment of Cardiac Support Device Group

One week after coronary artery ligation, the animals were randomly assigned to 1 of 3 groups: biodegradable device group (n = 7), nonbiodegradable device group (n = 8), and no-treatment (sham) group (n = 8). The heart was exposed via the re-thoracotomy through the fifth intercostal space. The cardiac support device was placed as described previously.[3-5] The no-treatment group was subjected to the same procedures as the support device groups, except for the device implantation (Fig. 1B and C).

MDCT

Contrast electrocardiography-gated MDCT was performed using a 16-row MDCT scanner (SOMATOM Emotion 16-slice configuration; Siemens) under general anesthesia. MDCT was performed before infarction, and at 1 week (pretreatment), 8 weeks, and 12 weeks after MI. Four beagles that had tachycardia at MDCT were excluded from the analysis because of compromised image quality (biodegradable group, n = 6; nonbiodegradable group, n = 6; no-treatment group,