Autologous skeletal myoblast transplantation in patients with nonacute myocardial infarction: 1-year follow-up

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Supplemental material is available online.

Objective: To determine the feasibility and safety of skeletal myoblast transplantation in patients with chronic myocardial infarction undergoing coronary artery bypass grafting.

Methods: Twelve patients with a previous myocardial infarction and ischemic coronary artery disease underwent treatment with coronary artery bypass grafting surgery and intramyocardial injection of autologous skeletal myoblasts cultured with autologous serum. Global and regional cardiac function was assessed by echocardiogram. Fluorine 18 fluorodeoxyglucose and nitrogen 13-ammonia positron emission tomography studies were used to determine cardiac viability and perfusion. A group of historical control patients (n = 14) treated with coronary artery bypass grafting surgery without myoblast transplantation was analyzed.

Results: The left ventricular ejection fraction improved from $35.5\% \pm 2.3\%$ (mean $\pm$ SEM) before surgery to $55.1\% \pm 8.2\%$ at 12 months ($P < .01$) in the myoblast group and from $33.6\% \pm 9.3\%$ to $38.6\% \pm 11\%$ in the control group. Regional contractility also improved in the myoblast group, particularly in cardiac segments treated with skeletal myoblasts (wall motion score index: 3.02 ± 0.17 at baseline vs 1.36 ± 0.14 at 12 months; $P < .0001$). Quantitative fluorine 18-fluorodeoxyglucose and nitrogen 13-ammonia positron emission tomography showed an increase in viability and perfusion 12 months after surgery both globally and in segments treated with myoblasts ($P = .012$ and $P = .004$). Skeletal myoblast implantation was not associated with adverse events or an increased incidence of cardiac arrhythmias.

Conclusions: In patients with previous myocardial infarction, treatment with skeletal myoblasts in conjunction with coronary artery bypass is safe and feasible and is associated with an increased global and regional left ventricular function, improvement in viability, and perfusion of cardiac tissue and no significant incidence of arrhythmias.

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Cardiac failure due to ischemic cardiomyopathy is one of the major health problems in the world because of its high prevalence and the high mortality and morbidity associated with it.¹ Myocardial infarction (MI) is associated with an irreversible loss of cardiomyocytes that leads to a process of cardiac remodeling with left ventricular (LV) enlargement and abnormal contractility that

Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
^{18}F -FDG	= fluorine 18–fluorodeoxyglucose
LV	= left ventricle
LVEF	= left ventricular ejection fraction
MI	= myocardial infarction
PET	= positron emission tomography
WMSI	= wall motion score index

eventually results in cardiac failure.² Although in the last few years several studies have suggested that the heart may have a certain capacity for regeneration, this is by no means enough to restore a normal function after MI.^{3,4}

Cell therapy has emerged as a potential alternative to heart transplantation for patients with end-stage cardiac disease.⁵ With the aim of replacing necrotic tissue, cells from different sources have been implanted in animal models of MI, including embryonic stem cells,⁶ fetal cardiomyocytes,⁷ skeletal myoblasts,⁸ hematopoietic stem cells,⁹ mesenchymal stem cells,¹⁰ or endothelial progenitor cells.¹¹ Most of these studies have invariably shown engraftment of donor cells and reconstitution of heart structures, ie, cardiomyocytes and blood vessels, and most of them have been associated with improved heart function. The results from clinical trials of intramyocardial cell transplantation with bone marrow mononuclear cells^{12,13} or bone marrow-derived AC133-positive cells¹⁴ for cardiac regeneration have been recently reported.

Among the different cell types used, skeletal myoblasts have several advantages: increased resistance to ischemia, autologous origin, ready access to the cell source, and the feasibility of ex vivo expansion of progenitor cells.^{15,16} However, the initial clinical studies have suggested that transplantation of skeletal myoblasts in patients with MI may be associated with an increased incidence of cardiac arrhythmias.^{17,18}

In this study, we have analyzed the results at 1 year in a group of patients with a history of MI treated with coronary artery bypass grafting (CABG) and skeletal myoblast transplantation. The safety of the procedure and its functional results were assessed by echocardiography, whereas perfusion and viability were determined by nitrogen 13 (^{13}N)-ammonia and fluorine 18–fluorodeoxyglucose (^{18}F -FDG) positron emission tomography (PET) studies and compared with a historical control group of patients treated with bypass surgery alone.

Patients and Methods**Patient Population and Study Design**

A total of 12 patients were included in the study. Inclusion criteria were (1) a history of MI greater than 4 weeks previously with akinetic or dyskinetic nonviable scar tissue, as demonstrated by a

lack of metabolic activity on ^{18}F -FDG PET; (2) indication for elective CABG; (3) age 30 to 80 years; and (4) a LV ejection fraction (LVEF) greater than 25%. Exclusion criteria included (1) an inability to obtain a myoblast cell culture, (2) a positive serologic test for human immunodeficiency virus or hepatitis, (3) a history of malignant arrhythmia or muscular dystrophy, and (4) abnormal liver or kidney function tests. The protocol and all the procedures were approved by the Institutional Review Board for Human Studies and Ethics Committee, the Regional Review Board for Clinical Trials With Human Subjects, and the Spanish Health Authorities. All patients signed an informed consent before entering the study.

Before surgery, all patients underwent ^{13}N -ammonia and ^{18}F -FDG PET scanning, echocardiography, and 24-hour Holter monitoring to determine the functioning and viability of the heart muscle. Laboratory studies included cardiac and liver enzymes and C-reactive protein. Studies were repeated 3 and 12 months after surgery. The preliminary results at 3 months have been reported previously.¹⁹

A control group of 14 matched patients who met the same inclusion criteria and received the same treatment, including bypass surgery, but who did not receive skeletal myoblast transplants were analyzed. This group underwent the same functional studies except for PET analysis.

Echocardiography Studies

Global and regional myocardial contractility was measured by 2-dimensional echocardiography by using a Sonos 5500 ultrasound system (Philips Medical Systems, Irvine, Calif). Regional LV wall motion analysis was performed as described by the Committee on Standards of the American Society of Echocardiography,²⁰ by dividing the LV into 16 segments and scoring wall motion for each segment as 1 (normal), 2 (hypokinesis), 3 (akinesis), or 4 (dyskinesis). The wall motion score index (WMSI) was calculated as the sum of the scores of the segments divided by the number of segments evaluated. WMSI was calculated for segments treated and not treated with cell implantation. LVEF was also calculated by using an automatic border detection system.²¹ Regional contractility was also assessed by color kinesis and tissue Doppler imaging for each segment. All studies were performed by 2 different observers. Reproducibility values within studies were 2.8 ± 6.4 mL (variation coefficient, 5.5%) for LV end-diastolic volume and 0.3 ± 4.6 (variation coefficient, 6.6%) for LVEF.

Tissue viability was assessed by low-dose dobutamine stress echocardiography for which dobutamine was given intravenously at an initial dose of $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ that was incremented every 3 minutes at $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ until a maximal dose of $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ was achieved. A continuous electrocardiogram was recorded, and semiquantitative regional function was blindly analyzed.

PET Studies

Myocardial blood flow and glucose metabolism were measured by PET scans before treatment and 3 and 12 months after treatment. The perfusion and metabolism studies were performed with a whole-body PET (ECAT EXACT HR+; Siemens/CTI, Knoxville, Tenn) as previously described.¹⁹

Autologous Skeletal Myoblast Cell Culture

Three to 4 weeks before CABG surgery, a muscle biopsy was obtained from the vastus lateralis under sterile conditions with the patient under local anesthesia (2% lidocaine hydrochloride) and processed immediately to obtain muscle progenitor cells as previously described.^{8,19} All patients underwent a plasma exchange the day before muscle biopsy was performed by using heparin as an anticoagulant. Cell cultures were incubated at 37°C and 5% carbon dioxide, and passage of the culture was performed at subconfluence to prevent myotube formation. During the first passage, preplating was applied to eliminate contamination of myoblasts with fibroblasts. Myoblasts were harvested after 3 to 4 passages for implantation. Myoblast purity was measured by flow cytometry after staining with monoclonal antibodies against human N-CAM (CD56), CD45, and desmin.²²

CABG Surgery and Cell Implantation

Three to 4 weeks after muscle biopsy, all patients underwent conventional aortocoronary bypass surgery. During cardiopulmonary bypass and after the conclusion of all graft anastomoses, immediately before removing extracorporeal circulation and while the heart was initiating spontaneous heartbeats, muscle progenitor cells (myoblasts) were injected subepicardially by multiple injections with an angled needle (Steriseal Ophthalmic canula, 23 gauge; Maersk Medical Ltd Redditch, UK) that allows tangential injection of cells under the epicardium. Myoblasts were implanted in segments previously identified by echocardiography as akinetic or dyskinetic in and around the infarct. Areas receiving cells were identified before surgery by echocardiogram, and these same areas were analyzed during follow-up to determine changes in regional contractility. Before myoblast implantation, a sample of the harvested myoblasts was used for microbiology cultures, including Gram staining to determine culture contamination. All patients were monitored with continuous telemetry throughout their hospital stay.

Statistical Analysis

Statistical analysis was performed with the SPSS 10.0 for Windows software package (SPSS Inc, Chicago, Ill). The normal distribution of quantitative variables was examined with the Kolmogorov-Smirnov test with the Lilliefors correction. Comparisons were performed with the paired *t* test for dependent variables and the Wilcoxon rank sum test, depending on the normality test. Differences between groups were analyzed with the χ^2 test (qualitative variables) or the *t* test for independent samples (quantitative variables). Comparisons for repeated measurements were performed with analysis of variance or the Friedman test. Descriptive analysis is presented as mean (SEM) for quantitative variables or median (interquartile range) for categorical variables.

Results

A total of 12 patients (11 men and 1 woman) with a mean age of 64.5 years (3.2 years) were included. Two patients were excluded from the analysis according to the criteria defined by the protocol (in 1 patient, myoblasts could not be cultured, and in another patient, the Gram staining before implantation was positive). The control group included 14

patients who had undergone CABG. There were no statistically significant differences between the characteristics of both groups (Tables E1 and E2).

All patients underwent CABG as scheduled. The infarct area was documented as nonviable by dobutamine echocardiography and ¹⁸F-FDG PET in patients undergoing myoblast transplantation (viability was assessed only by dobutamine echocardiography in the control group). The mean size of the muscle biopsy was 9.45 g (5.5-14 g), and the mean volume of autologous serum obtained was 1.735 mL (800-2.135 mL). After a median of 23 days (18-26 days) in culture, a mean of 221×10^6 ($105\text{-}390 \times 10^6$) myoblasts were obtained with a purity of 65.6% (48%-92%; percentage of CD56⁺ cells/CD45⁺ cells). An average of 5 mL (3.5-6 mL) of solution containing skeletal myoblasts was injected by multiple injections as previously described.¹⁹ The average concentration of myoblasts was $50 \times 10^6/\text{mL}$, and the number of injections varied between 5 and 15. The median number of segments treated with myoblasts was 7 (4-10): anterior wall, *n* = 6; inferior wall, *n* = 3; and apical region, *n* = 1. No significant differences were found between patients and controls regarding the surgical procedure (Table E2).

Adverse Events

In the group of patients treated with myoblasts, 2 patients were readmitted to the hospital with heart failure: 1 at 5 months after surgery and 1 at 12 months after surgery, also having recurrence of angina. One patient had episodes of paroxysmic third-degree atrioventricular block requiring pacemaker implantation 5 months after surgery. Before surgery, nocturnal episodes of complete atrioventricular block were detected in this patient by Holter monitoring. Finally, amyotrophic lateral sclerosis developed in 1 patient 6 months after surgery. The median number of ventricular premature beats was 13 (309), 11 (23), and 34 (759) at baseline and 3 and 12 months, respectively (*P* = .386). No other malignant arrhythmias were detected, and no implantable defibrillators were required. Plasma exchange was not associated with adverse events. Muscle biopsy was associated with a minor local bleeding episode in 1 patient 12 hours after the biopsy.

In the control group, 4 patients experienced heart failure and were readmitted to the hospital. Two of them were treated with a resynchronization pacemaker, in 1 case with internal defibrillator capabilities.

Echocardiography Results

At 12 months after surgery, a significant increase in LVEF and a decrease in LV diameters and volumes were observed (Table E3). LVEF by automatic border detection increased from 40.38% (2.42%) at baseline to 54.33% (2.46%) and 60.83 (3.5%) at 3 and 12 months after surgery, respectively (*P* < .001). Both at 3 and 12 months, there was a significant

TABLE 1. Regional contractility studies (WMSI)

Variable	Baseline	3 mo	12 mo	P value
Global				
Control	2.1 (0.51)		2.02 (0.40)	.620
Myoblasts	1.8 (0.14)	1.25 (0.08)*	1.15 (0.05)	.001
Treated segments				
Control	2.99 (0.31)		2.82 (0.30)	.220
Myoblasts	3.02 (0.17)	1.64 (0.16)*	1.36 (0.14)	<.001
Untreated segments				
Control	1.65 (0.50)		1.55 (0.4)	.425
Myoblasts	1.29 (0.08)	1.05 (0.04)*	1.02 (0.01)	.041

Data are mean (SEM). WMSI, Wall motion score index. * $P < .05$ between baseline and 3 months. There were no differences between 3 and 12 months.

improvement in regional contractility assessed by WMSI in the group of patients treated with myoblast implantation. A statistically significant improvement was observed when we analyzed segments treated with revascularization alone or with revascularization and skeletal myoblasts (Table 1).

In the control group, the increase in LVEF 12 months after surgery did not reach statistical significance, and no significant changes were detected in remodeling parameters or in the WMSI (Tables 1 and E3). The changes in LVEF and in LV diameters were significantly different between the group of patients treated with myoblasts and the control group (Figures 1 and 2).

Myocardial Perfusion and Viability PET Studies

The ^{18}F -FDG and ^{13}N -ammonia PET were performed before surgery (1-5 days) and at 3 and 12 months after surgery. A global increase in ^{18}F -FDG uptake was observed at 3 and 12 months after surgery compared with baseline values. This increase was more pronounced when only segments treated with myoblasts were analyzed. Perfusion studies with ^{13}N -ammonia showed a statistically significant im-

Figure 2. Median percentage of change in LV diameters and volumes in the group of patients treated with myoblasts and in the control group. LVEDV, Left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter.

provement at 12 months but not at 3 months. As described in the viability studies, the improvement was particularly observed in segments treated with myoblasts (Table 2).

Discussion

The results of our study indicate that transplantation of autologous skeletal myoblasts in patients with a history of MI as adjuvant therapy to bypass surgery is feasible and safe and is associated with an improvement in LVEF and an increase in the viability and perfusion of the nonviable myocardium. This improvement appears mainly in the area of implantation, as indicated by ^{18}F -FDG and ^{13}N -ammonia PET.

Figure 1. LVEF before and 12 months after CABG in patients treated with myoblasts and in the control group. Results represent individual values for each patient as well as the mean (SEM). $P < .001$ between changes observed in the control group and patients treated with myoblasts.

TABLE 2. Myocardial viability and perfusion studies (PET)

Variable	Baseline	3 mo	12 mo	P value
Global				
Ammonia	0.47 ± 0.03	0.50 ± 0.02	0.65 ± 0.06	.019
¹⁸ F-FDG	0.158 ± 0.02	0.270 ± 0.01*	0.267 ± 0.02	.019
Treated segments				
Ammonia	0.40 ± 0.05	0.44 ± 0.03	0.62 ± 0.05†	.009
¹⁸ F-FDG	0.126 ± 0.02	0.231 ± 0.01*	0.230 ± 0.02	.004
Untreated segments				
Ammonia	0.59 ± 0.05	0.62 ± 0.04	0.67 ± 0.07	.215
¹⁸ F-FDG	0.170 ± 0.05	0.284 ± 0.01*	0.280 ± 0.05	.930

PET, Positron emission tomography; ¹⁸F-FDG, fluorine 18-fluorodeoxyglucose.

*P < .05 between baseline and 3 months. †P < .05 between 3 and 12 months.

It has been demonstrated in small- and large-animal models of MI that skeletal myoblasts transplanted into the myocardium are able to engraft and differentiate into myofibers and, under certain circumstances, may acquire characteristics of cardiomyocytes (see review¹⁵). In the clinical setting, transplantation of skeletal myoblast results in cell engraftment and contributes to improvement of cardiac function in patients with MI.^{17,18} However, despite a large number of studies, the mechanisms by which myoblasts contribute to cardiac function remain unknown. Some studies have suggested that myoblasts acquire certain characteristics of cardiac muscle after transplantation into the myocardium (presence of cardiac-specific myosin heavy chain and connexin 43).²³ Moreover, at least in vitro, skeletal fibers and cardiac muscle can form electromechanical junctions.²⁴ Nevertheless, overwhelming evidence indicates that skeletal myoblasts do not transdifferentiate into cardiomyocytes.^{25,26} The elastic properties of implanted fibers and/or the secretion of certain growth or survival factors, contributing to remodeling or to recruitment of circulating or local cardiac stem cells, have been implicated as potential mechanisms involved in the observed benefit of myoblast transplantation in animal studies.¹⁵

The number of skeletal myoblasts transplanted in the different studies have varied from a few million to more than a billion cells.^{17,18} On the basis of preclinical data suggesting that functional improvement is correlated with the number of cells²⁷ and the fact that myoblast retention after transplantation is less than 5%,²⁸ the number of cells injected in our study could be considered to be in the lower range. However, the number of cells injected in our patients was similar to the number of cells injected in 2 other studies in which engraftment of myoblasts was demonstrated.^{18,29} Although proof of engraftment was not obtained in our patients, the results of these studies and the increase in ¹⁸F-FDG uptake in the area where the cells had been im-

planted suggest that probably enough cells were injected to obtain a successful engraftment.

The functional improvement observed in our patients is encouraging but is certainly overshadowed by the fact that patients underwent both skeletal myoblast transplantation and bypass surgery to the same area that received cells. This is a major limitation of our study. As we have described, several approaches have been used to try to differentiate the functional benefit derived from myoblast transplantation from the potential effect of bypass surgery. Although the value of using a control group for comparison is limited and only randomized trials can establish whether the improvement in cardiac function is due to cell therapy, the results of the comparison between patients and controls clearly suggest that transplantation of myoblasts is associated with an increase in LVEF for up to 1 year after surgery. Furthermore, the differences observed in end-systolic and end-diastolic diameters suggest that skeletal myoblasts could limit ventricular remodeling, probably by releasing molecules capable of altering the extracellular matrix.³⁰ The lack of uptake of ¹⁸F-FDG PET as an inclusion criterion excludes the possibility that improved cardiac function could be due to revascularization of hibernating tissue. Also, the increase in ¹⁸F-FDG uptake mainly in areas where myoblasts were injected, along with the improvement in WMSI in the same areas, suggests that the benefit observed is, at least in part, due to the injected myoblasts.

It is interesting to note that a statistically significant increase in the uptake of ¹³N-ammonia was observed 12 months after surgery and that this was more pronounced in areas where myoblasts had been implanted. As described previously, increased perfusion is associated with increased ¹³N-ammonia uptake, and this suggests an increase in vascularization of the infarct area. Although histological analysis would be required to demonstrate an increase in angiogenesis or vasculogenesis in patients who have undergone transplantation with myoblasts, these results suggest that this mechanism may underlie the benefit observed in our patients. In a recent study in patients receiving skeletal myoblast transplants at the time of LV assist device implantation, the morphological analysis suggested an increase in angiogenesis in the explanted heart at the time of heart transplantation.¹⁸

An important finding in our patients is the lack of cardiac arrhythmias observed—a finding that contrasted with other recent studies,^{17,18} in which 4 of 10 patients with old MIs treated with CABG and intramyocardial injection of skeletal myoblasts required implantation of an automatic internal cardioverter-defibrillator.¹⁷ The reason for these arrhythmias is at present unknown, but it could be related to electrical reentry circuits due to the lack of established gap junctions between skeletal myoblasts and cardiomyocytes,²⁵ to the number and/or volume of cells implanted, or to other

currently unknown mechanisms. We cannot rule out that the absence of arrhythmias in our patients is not due to revascularization of the infarct area, to the use of autologous serum (the use of bovine serum in cell cultures has been associated with inflammation and/or killing of the cells³¹), or even to patient selection, because the baseline LVEF was better in our patients than in either of the previous studies.^{17,18} In a very recent study, the finding that skeletal myoblasts do not establish gap junctions with cardiomyocytes has been hypothesized as a mechanism to prevent the generation of dangerous premature beats²⁶; this is consistent with our own clinical observations.

In conclusion, our results suggest that cell transplantation with bypass surgery is associated with improved cardiac function, increased tissue viability, and lack of side effects, thus resulting in a promising therapy for patients with heart failure. These results warrant further clinical research, including randomized studies.

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TABLE E1. Baseline characteristics of patients and controls

Variable	Myoblast group	Controls	P value
n	10	14	
Age (y)	64.5 (3.3)	60.4 (9.5)	.321
Male	9 (90%)	12 (85.7%)	.754
Concurrent risk factors			
Hypertension	4 (40%)	7 (50%)	.697
Diabetes mellitus	3 (30%)	6 (42%)	.889
Hyperlipidemia	4 (40%)	8 (57.1%)	.889
Current cigarette use	9 (90%)	8 (57.1%)	.172
Infarct-related artery			
Left anterior descending	7 (70%)	6 (42.9%)	.240
Right coronary	3 (30%)	8 (57.1%)	.240
Primary therapy for MI			
Fibrinolysis	6 (60%)	4 (28.6%)	.211
Angioplasty	2 (20%)	9 (64.3%)	.051
Medical therapy	2 (20%)	1 (7.1%)	.550
Time from MI to CABG (mo)	21.5 (118)	19.9 (23)	.136
Echocardiographic data			
LVEF	35.6 (2.3)	33.4 (9.1)	.328
LVEDV	175 (39.3)	221 (101)	.167
LVESV	99.1 (26.8)	141 (68.3)	.087
LVEDD	60.8 (4.1)	65 (12.4)	.441
LVESD	45.7 (5.4)	50.8 (12.2)	.319
Current therapy			
ACEI/ARB	10 (100%)	10 (71.4%)	.678
ASA	10 (100%)	14 (100%)	0.889
β -blockers	7 (70%)	8 (57.1%)	.388
Statins	10 (100%)	9 (65%)	.053
Diuretics	7 (70%)	9 (65%)	.678

Data are n (%) or mean (SEM). *MI*, Myocardial infarction; *CABG*, coronary artery bypass grafting; *ACEI*, angiotensin-converting enzyme inhibitor; *LVEF*, left ventricular ejection fraction; *LVEDV*, left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume; *LVEDD*, left ventricular end-diastolic diameter; *LVESD*, left ventricular end-systolic diameter; *ARB*, angiotensin receptor blocker; *ASA*, acetylsalicylic acid.

TABLE E2. Surgical data of patients and controls

Variable	Myoblast group	Controls	P value
No. grafts			
2	2 (20)	1 (7.1)	.550
3	4 (40)	7 (50)	.280
>3	4 (40)	6 (42.9)	.211
Revascularization to infarct area	9 (90)	13 (92)	0.786
Aneurysmectomy	1 (10)	1 (7.1)	0.926
Bypass duration	128.9 (18.5)	157 (64.2)	.298
Maximal CK levels (UI/L)	806 (127.3)	782 (575)	.882
Maximal CK-MB levels (UI/L)	26.9 (2.7)	35.7 (38.1)	.433
Maximal troponin levels (ng/mL)	2.86 (1.85)	4.77 (4.7)	.347

Data are mean (SEM). *CK*, Creatine kinase; *CK-MB*, creatinine kinase isoenzyme MB.

TABLE E3. Echocardiographic results

Variable	Baseline	12 mo	P value
LVEF			
Control	33.6 (9.3)	38.6 (11)	.08
Myoblasts	35.6 (5.6)	55.1 (8.2)	<.01
LVEDV			
Control	221 (101.6)	223 (64.1)	.91
Myoblasts	175 (39.3)	166.1 (30)	.63
LVESV			
Control	141 (68.3)	125 (55.8)	.36
Myoblasts	99.1 (26.8)	69.1 (15.8)	.01
LVEDD			
Control	65 (12.4)	65.8 (12.1)	.69
Myoblasts	60.8 (4.1)	53.5 (3.2)	<.01
LVESD			
Control	50.8 (12.2)	50.5 (11.9)	.89
Myoblasts	45.75 (5.4)	38.6 (3.5)	<.01

Data are mean (SEM). *LVEF*, Left ventricular ejection fraction; *LVEDV*, left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume; *LVEDD*, left ventricular end-diastolic diameter; *LVESD*, left ventricular end-systolic diameter.