Coronary artery bypass grafting without cardiopulmonary bypass has become an increasingly practiced technique for myocardial revascularization. This method generally uses local coronary occlusion, resulting in a brief period of myocardial ischemia. Although the effects of ischemia on regional myocardial function have been studied extensively in animal models, the significance of limited periods of ischemia on human heart function is not well defined. The development of regional ultrasonic dimension analysis by Theroux and associates allowed accurate determination of changes in regional myocardial function. Using this technology, Edwards et al characterized the geometric alterations in myocardium during ischemia as a time-dependent stretch of myocardial segments called “creep.” Glower and associates showed that the reversal of diastolic creep correlated with recovery of systolic function after reversible ischemic injury.

The purpose of this investigation is to define the effects of acute transient myocardial ischemia on regional systolic function in the face of chronic ischemia caused by coronary artery disease in humans.

**Experimental Preparation and Data Acquisition**

Following protocol approval by the institutional review board, all patients scheduled for left internal mammary artery to left anterior descending coronary artery (LAD) bypass between January 1998 and April 1998 were given an opportunity to participate in this study. A total of 11 patients gave informed consent, and data collection was completed in 8 patients (the Table). Conversion to an open procedure \( n=1 \) and equipment malfunction \( n=2 \) excluded 3 patients.

Anesthesia was induced with fentanyl \( 8 \) to \( 10 \) \( \mu \)g/kg IV, Versed \( 2 \) to \( 5 \) mg IV, Amidate \( 3 \) mg/kg IV, and vecuronium \( 0.1 \) to \( 2 \) mg/kg IV. All patients were maintained on a nitroglycerin infusion \( 0.5 \) mg \( \cdot \) kg\(^{-1} \cdot \) min\(^{-1} \), but no other vasoactive drugs were used. Patients were placed in a supine position with the left side of the chest slightly elevated as per routine for minimally invasive direct CABG. Three additional ECG leads (right arm, left arm, and left leg) were placed for attachment to the data collection system. The procedure was performed through a small left anterior thoracotomy. After harvest of the left internal mammary artery and preparation for grafting, the remaining instrumentation specific to the study protocol was placed as follows. A single 7F left ventricular pressure catheter (Millar) was inserted through an 18-gauge needle puncture near the ventricular apex. Two subepicardial cylindrical ultrasonic dimension transducers (Sonometrics) were placed 15 to 20 mm apart in the
minor axis plane to subtend the myocardial region supplied by the LAD. The crystals were secured with 5 to 0 prolene sutures to prevent dislodgement. Analog data (200 Hz) collected for 8 seconds were discreet time points during the procedure. These points were (1) before LAD occlusion (baseline), (2) just before LAD release (occlusion, 10 to 24 minutes), and (3) before incision closure (reperfusion, 7 to 10 minutes total). Analog recordings were converted to digital data points by a sonomicrometer (Sonometrics). The sonomicrometer has a range of measurement from 10 to 120 mm, with the smallest measurable change in distance being 0.024 mm. This is linear throughout the entire measurement range. At the conclusion of data collection, all monitoring devices were removed, and the patients’ wounds were closed as per standard practice.

Data Analysis and Statistical Comparison
Digital data were transferred into Microsoft Excel for further analysis. The cardiac cycle was defined by use of the first derivative of the pressure/time interval (dP/dt) as described previously, and pressure-dimension loops were generated by plotting all continuous measurements recorded for 8 seconds at each given time point. Percent systolic shortening (%SS) was calculated using this formula: 

\[
%SS = \frac{(EDL - ESL)}{EDL} \times 100
\]

where EDL is end-diastolic length and ESL is end-systolic length.

Linear regression analysis was used to compare the decrease in percent systolic shortening to the degree of native coronary artery stenosis. Paired t tests and the Wilcoxon signed-rank test were used to compare values at different time points. Numerical data were expressed as mean±SD. Statistical significance was defined as \( P < 0.05 \).

Results
All patients tolerated the procedure well, and no complications occurred. Patients in the study group had normal left ventricular function as assessed on ventriculography. LAD runoff was judged as good (n=2) or excellent (n=6) on the basis of preoperative angiographic interpretation by the surgeon. Stenosis of the LAD ranged from 70% stenosis to total occlusion (n=2). Collateral arterial supply was graded as minimal (n=5), moderate (n=1), or extensive (n=2). This was judged by the amount of back bleeding from the LAD during proximal occlusion after the arteriotomy was made. No patient developed significant ST-segment elevation during the operation, nor were any significant hemodynamic changes noted.

Duration of LAD occlusion was 15.9±4.4 minutes (range, 12 to 26 minutes). Regardless of occlusion length, there was a significant decline in systolic shortening in patients with nonoccluded LADs from 5.8±0.8% to 1.8±0.8% (n=6, \( P < 0.02 \)). In all cases, dysfunction resolved completely after reperfusion (mean, 8.6±2.4; range, 6 to 13 minutes after

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EDL indicates end-diastolic length; C, control; I, ischemia; and R, reperfusion.
release of occlusion). Pressure-dimension loops (Figure 1) narrowed during ischemia but returned to baseline and revealed no diastolic creep as evidenced by return of end-diastolic length (the Table).

Linear repression analysis revealed a significant inverse correlation between degree of coronary stenosis and percent decrease in systolic shortening \( (P<0.02) \) (Figure 2).

**Discussion**

Detrimental effects of ischemia on regional myocardial function have been well documented.\(^1-11\) Previous studies have clearly shown that with the loss of active shortening during ischemia, regional systolic stress increases, contributing to regional ischemic dysfunction and facilitating passive elongation of ischemic myocardium.\(^6,7\) These regional myocardial geometric changes characterized by progressive increases in end-diastolic segment length and decreased end-diastolic wall thickness occur as a time- and load-dependent change identified as creep.\(^5\) Owen et al\(^7\) subsequently showed that significantly increased end-diastolic length persisted for hours after only a 15-minute period of regional ischemia in dogs and that late functional recovery correlated primarily with reversal diastolic creep.

The present study involved measurement of regional systolic function in chronically ischemic human myocardium that was then subjected to a period of acute ischemia during the time of local coronary occlusion necessary for off-pump bypass. A measurable decline in regional left ventricular systolic function was observed, as evidenced by a reduced percent systolic shortening. Pressure-dimension loops confirmed diminished shortening fraction but did not demonstrate evidence of the time-dependent stretch of myocardial segments or diastolic creep. Furthermore, these changes were more significant with lesser degrees of coronary artery stenosis and presence of established collaterals. After restoration of blood flow, systolic shortening returned to baseline within minutes. In contrast, previous animal studies have demonstrated prolonged myocardial dysfunction after comparable periods of regional ischemia.\(^5-7\)

The results of this investigation demonstrate an increased tolerance to ischemia in humans with coronary artery disease. This can be explained in part by the slowly progressive nature of coronary lesions caused by atherosclerosis, in contrast to the normal arteries present in animal studies. The slow disease progression allows development of collaterals and increased ischemia tolerance. This is supported by the inverse correlation noted between the degree of stenosis and decrease in systolic shortening in the present study. In addition, chronic coronary stenosis may induce a “preconditioned” state, rendering the myocardium more tolerant to acute occlusion.\(^11\)

The clinical significance of this investigation is 2-fold. First, myocardial ischemia of the duration necessary to perform a coronary anastomosis does not appear to result in any long-lasting change in myocardial function. Therefore, permanent injury to the myocardium is unlikely to occur. Second, local occlusion does result in transient myocardial dysfunction, the degree of which is greater with lesser coronary stenosis and collaterals. Although no patient in this study had hemodynamic compromise during coronary occlusion, this is a well-known albeit rare complication. These data provide evidence that other strategies, such as coronary shunting, rather than local occlusion might be advised in patients with only moderate coronary stenoses and large myocardial areas at risk.

**Acknowledgment**

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**References**


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**Figure 2.** Pressure-dimension loops from control state, during ischemia, and after reperfusion derived from 1 patient study.
Regional Left Ventricular Systolic Function in Humans During Off-Pump Coronary Bypass Surgery

Philip M. Brown, Jr, Victor B. Kim, Bret J. Boyer, Robert M. Lust, W. Randolph Chitwood, Jr and Joseph R. Elbeery

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