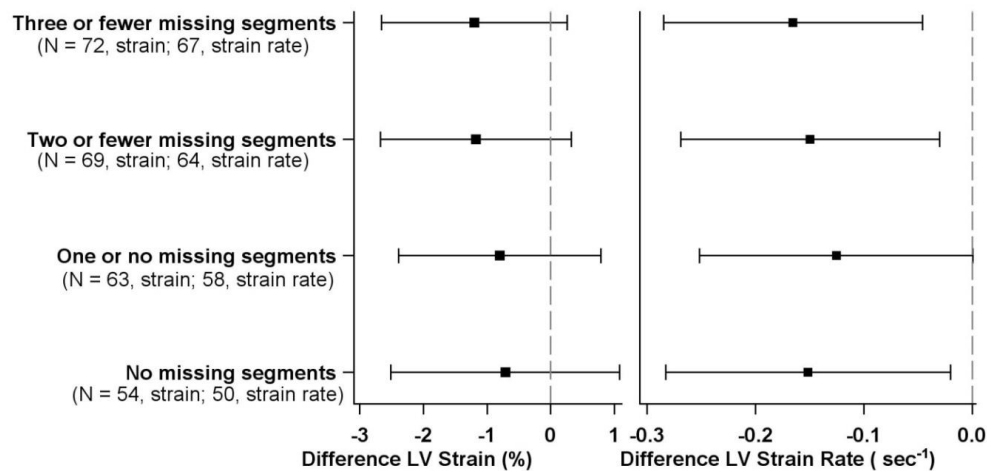


## Supplemental Digital Content 4

### Supplemental Results

#### *Echocardiographic data analysis*

A sensitivity analysis compared analyses of strain and strain rate in patients with 18, 17 or more, and 16 or more “acceptable” segments with the final study results (which included 15 or more “acceptable” myocardial segments). Results from the sensitivity analysis were consistent and are shown in Figure 1 below. Our final analysis of strain and strain rate data with 15 or more “acceptable” myocardial segments is reported in the main text (Table 3 and Figure 3).



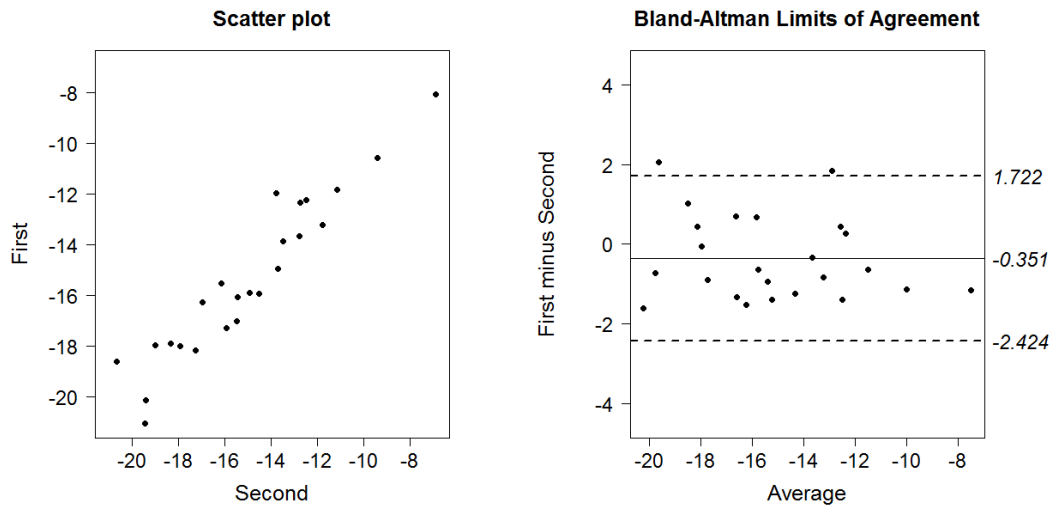
**Fig. 1.** A comparison of the difference<sub>(HNC minus standard)</sub> (95% confidence interval) in global left systolic longitudinal strain and strain rate using individual analyses with all 18 (no missing) segments, 17 of 18 (one or no missing) segments, 16 of 18 (two or fewer missing) segments, and 15 of 18 (three or fewer missing) segments, respectively, demonstrates results consistent with the primary analysis. HNC = Hyperinsulinemic normoglycemic clamp; LV = left ventricle

Of 72 patients in the primary analysis of left ventricular strain, 54 (75%) had all (18 of 18) myocardial segments deemed “acceptable”, 9 (13%) had 17 of 18 segments deemed “acceptable,” 6 (8%) had 16 of 18 segments deemed “acceptable,” and 3 patients (4%) had 15 of 18 segments deemed “acceptable.” Of 67 patients in the primary analysis of left ventricular strain rate, 50 (75%) had all (18 of 18) myocardial segments deemed “acceptable,” 8 (12%) had 17 of 18 segments deemed “acceptable,” 6 (9%) had 16 of 18 segments deemed “acceptable,” and 3 patients (4%) had 15 of 18 segments deemed “acceptable.”

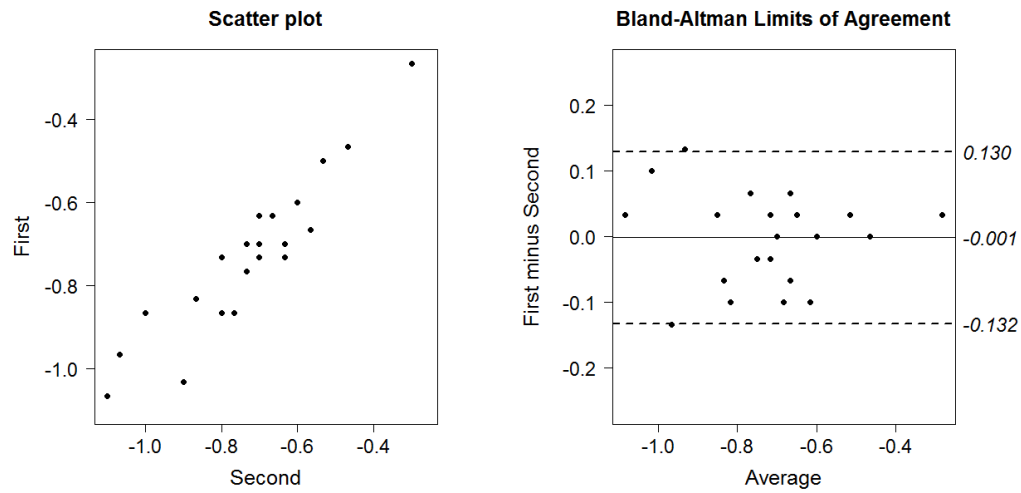
Right ventricular strain analysis was assessed from the transesophageal echocardiographic view with the image centered on the right ventricle. Of the 95 patients with echocardiographic data, 54 patients had acceptable echocardiographic images for right ventricular strain and strain rate analysis (a minimum of 5 of 6 acceptable myocardial segments). All patients had complete assessment of the right ventricular free wall. Of these 54 patients, 53 (98%) had all six myocardial segments deemed “acceptable” and 1 (2%) had 5 of 6 myocardial segments deemed “acceptable.”

### ***Calculation of Intra-observer variability using Bland-Altman Limits of Agreement***

Intraobserver variability assessed using Bland-Altman limits of agreement is shown in Fig. 2 and 3.



**Fig 2.** Intraobserver variability of left ventricular strain analysis demonstrated with Bland-Altman plots. First = first analysis of strain; Second = repeated analysis of strain to assess intraobserver variability.



**Fig. 3.** Intraobserver variability of left ventricular strain rate analysis demonstrated with Bland-Altman plots.

### ***Calculation of Intraobserver variability using binomial exact method***

The proportion of differences (first–second) within acceptance limits of  $\pm 10\%$  were moderate to good at 0.79 (0.58, 0.93) for strain and 0.75 (0.53, 0.90) for strain rate. The proportions of differences were 100% within acceptance limits of  $\pm 20\%$  for both strain and strain rate.