(p = NS). There was no difference in reported adverse events.

In conclusion, compared with conventional CA guidance, FS alone was found to be an equally safe and effective protocol, with similar immediate procedural and 6-month MACE rates, as well as similar clinical outcomes for PCI, and had a significantly lower radiation at the source.

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Risk of New-Onset Diabetes and Cardiovascular Risk Reduction From High-Dose Statin Therapy in Pre-Diabetics and Non–Pre-Diabetics

An Analysis From TNT and IDEAL

Statins reduce coronary and cerebrovascular events in primary and secondary prevention. More intensive statin therapy compared with moderate-intensity statin therapy decreases risk even further (1). Therefore, the 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend high-intensity statin therapy in high-risk patients. This recommendation is partly on the basis of the documented safety of higher doses. However, meta-analyses have reported a slight increase in the risk of new-onset diabetes (NOD) with statin therapy over placebo; this risk increases by an additional 12% with high-intensity therapy (2).

Fasting blood glucose (FBG) >100 mg/dl is a strong predictor of NOD; however, the incidence of NOD during statin therapy in patients with pre-diabetes (PD), which is defined as a FBG of 100 to 126 mg/dl, compared with those with normal glucose levels, has not been previously reported. We describe the incidence of NOD in patients with and without PD at baseline from the TNT (Treating to New Targets) and IDEAL (Incremental Decrease in Clinical Endpoints Through Aggressive Lipid Lowering) randomized clinical trials.

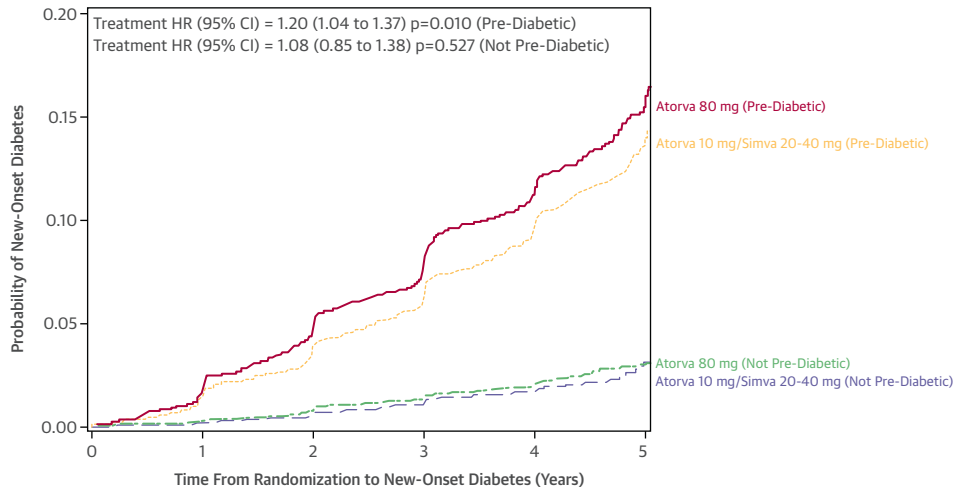
We pooled patients without diabetes at baseline from both the TNT and IDEAL trials (3,4). The TNT study randomized 10,001 patients with documented coronary heart disease to atorvastatin 10 or 80 mg/day and followed them for a median of 4.9 years (3). The IDEAL study randomized 8,888 patients with a previous myocardial infarction (MI) to simvastatin 20 to 40 mg/day or atorvastatin 80 mg/day with a median follow-up of 4.8 years (4).

The primary endpoint of our analysis was the composite of coronary heart disease death, nonfatal MI, resuscitated cardiac arrest, and stroke. NOD was defined prospectively as at least 2 post-baseline FBG measurements ≥126 mg/dl or at least 1 post-baseline FBG ≥36 mg/dl above baseline (5). FBG was measured at each 12-month visit in TNT and at randomization and at the end of study in IDEAL. We also included patients who had NOD identified through adverse event reporting or patients who received new concomitant diabetic medication.

Of the total 15,056 patients from both trials without diabetes at baseline, 5,924 (39%) had PD, and 9,132 (71%) patients did not. PD and non-PD patients were evenly balanced across the statin treatment arms. Compared with those without PD, PD patients were more likely to be older, to be men, to have metabolic syndrome, to have higher baseline blood pressure, and to have a history of hypertension. PD patients also had, on average, a higher body mass index, higher FBG, higher triglyceride levels, and lower levels of high-density lipoprotein cholesterol.

During the mean 5-year follow-up, 14.2% of PD patients developed NOD compared with 2.9% of patients without PD (hazard ratio [HR]: 5.29, 95% confidence interval [CI]: 4.6 to 6.1; p <0.001). As shown in **Figure 1**, the incidence of NOD was not time-dependent, and occurred at the same rate throughout the trial. In patients with PD, the risk of NOD was higher in the high-intensity statin group (HR: 1.20, 95% CI: 1.04 to 1.37; p = 0.010). In patients without PD, the difference between the high- and moderate-intensity treatment groups was not statistically significant (HR: 1.08, 95% CI: 0.85 to 1.38; p = 0.527).

FIGURE 1 Effect of Pre-Diabetes on Incidence of New-Onset Diabetes



Kaplan-Meier event-free survival curves from the TNT and IDEAL trials showing new-onset diabetes (NOD) in pre-diabetics and non-pre-diabetics by treatment group. IDEAL = Incremental Decrease in Clinical Endpoints Through Aggressive Lipid Lowering; TNT = Treating to New Targets.

The primary composite endpoint was greater for the PD group compared with the non-PD group (10.5% and 9.6%, respectively; HR: 1.11, 95% CI: 1.00 to 1.23, p = 0.05). High-intensity statin treatment compared with moderate-intensity statin treatment reduced cardiovascular events in patients with PD (9.5% vs. 11.5%; HR: 0.82, 95% CI: 0.70 to 0.96; p = 0.014) and without PD (8.9% vs. 10.2%; HR: 0.87, 95% CI: 0.76 to 0.99; p = 0.038).

In summary, in this analysis of 2 large cohorts of patients without diabetes who were taking statins, PD was a very strong predictor of the development of NOD during the 5-year follow-up, with high-intensity statin therapy, compared with moderate-intensity statin therapy, significantly increasing the risk of NOD in the PD group, but not in the non-PD group. In contrast, the risk of cardiovascular events was only marginally greater in the PD group compared with the non-PD group, and high-intensity statin therapy compared with moderate-intensity statin therapy significantly reduced cardiovascular events in both groups.

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JACC VOL. 65, NO. 4, 2015
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Differences in Experience With a New Delivery Device for LAA Ligation Among Various U.S. Centers

The Lariat suture delivery device (SentreHeart, Redwood City, California) has been used to exclude the left atrial appendage (LAA). Thus far, there have not been any randomized controlled trials or large multicenter experiences reported on the device. Price et al. made an attempt to describe their multicenter experience with the Lariat device as part of the U.S. Transcatheter LAA Ligation Consortium on the safety and efficacy of transcatheter ligation of the LAA for stroke prevention in atrial fibrillation (1).

It is an important study that showed how a procedure could have suboptimal outcomes if not executed properly. In addition, it was fraught with several issues that deserve attention and were not discussed in the accompanying editorial. Their sample size reflected a small portion (7.7%) of the 2,000-plus cases that were performed in the country at the time of this publication. Their experience might not be a reflection of the performance of this device across other centers that have more experience. The majority of the participant institutions seemed to have limited experience with this device (mean of 19 cases per institution). There was no mention of the selection criteria for the participating centers and the experience and training of the operators, and the exclusion and inclusion criteria were not defined. It is not clear what percentage of these patients underwent the procedure on a compassionate basis (outside of standard eligibility as recommended by the manufacturer and mentioned in other studies) (2,3). This muticenter experience is far from being a true consortium.

The bleeding and major complication rates reported by the investigators are concerning, but these rates do not reflect the clinical experience of other operators in the country from single-center experiences (3,4). In a quick survey, conducted in 11 U.S. sites (6 academic centers and 5 community-based practices with a mean 40 patients per institution) that included 441 patients, acute closure was seen in 420 patients (95%); an incidence of bleeding of >500 ml was seen in 10 patients (2.2%); 9 patients (2%) needed blood transfusions; and 6 patients (1.3%) needed open heart surgery for cardiac perforation. Most of these complications were seen early on, during the use of a 18-gauge Pajunk needle (Pajunk Medical Systems, Norcross, Georgia) for pericardial access. Subsequently, operators switched to a micropuncture needle in a total of 231 (52.3%) patients. There were no complications related to pericardial access. Three hundred sixty-three patients (82.3%) underwent follow-up transesophageal echocardiographies, with 32 patients (7.2%) showing a leak during follow-up transesophageal echocardiography at >1 mm. Eight patients (2%) had delayed thrombus formation at the ligation site. Five patients (1.1%) had delayed pericardial effusion, and 9 patients (2%) had delayed pleural effusions. No deaths were noted in any of these patients. It should also be noted that the initial results from 1 of the participating centers in the U.S. Transcatheter LAA Ligation Consortium reported their experience, which was vastly different from the recent registry. This discrepancy suggests the wide variation in adherence to the procedure as previously described (2,5), patient selection, and evolution of the technique. In addition, the investigators mentioned the use of a micropunture needle for pericardial access but did not indicate the percentage of patients in which this needle was used. From our survey, the incidence of using the micropuncture needle for pericardial access was in 52.3%, with no evidence of bleeding or any other major complications.

Given the limitations noted from the accompanying editorial and the contrary experience of the surveyed centers, the results of this study should be evaluated with caution, because these findings might not be reflective of the global safety and effectiveness profile of the Lariat procedure in experienced hands for appropriately selected patients. A prospective, rigorous clinical investigation is required to prove the risk and/or benefit profile of this therapy, which will be forthcoming in the near future.

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