Improving the Pharmacological Regimen for Patients With Diabetes Mellitus

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Type 2 diabetes mellitus afflicts nearly 17 million people in the United States, and prevalence rates are expected to double within 2 decades. Although there has been a downward trend in cardiovascular morbidity and mortality in recent years, cardiovascular disease remains the leading cause of death among patients with diabetes. This observation has led many to reevaluate current treatment goals and pharmacologic regimens for at-risk patients with type 2 diabetes mellitus. This review focuses on the current adjunctive pharmacologic treatment regimen that is well-suited for these patients. [Rev Cardiovasc Med. *2004;5(3):139–147*]

Key words: Diabetes mellitus • Coronary artery disease • Myocardial infarction • Restenosis

One hundred million people worldwide have a history of diabetes mellitus. Approximately 12 million individuals have been diagnosed with diabetes mellitus in the United States; however, conservative estimates suggest that one third of the US diabetic population remains undiagnosed.[1] Furthermore, an additional 40 million persons have insulin resistance syndrome and thus are at heightened risk for developing type 2 diabetes mellitus (DM).[2] These numbers are projected to double in the next decade, primarily among

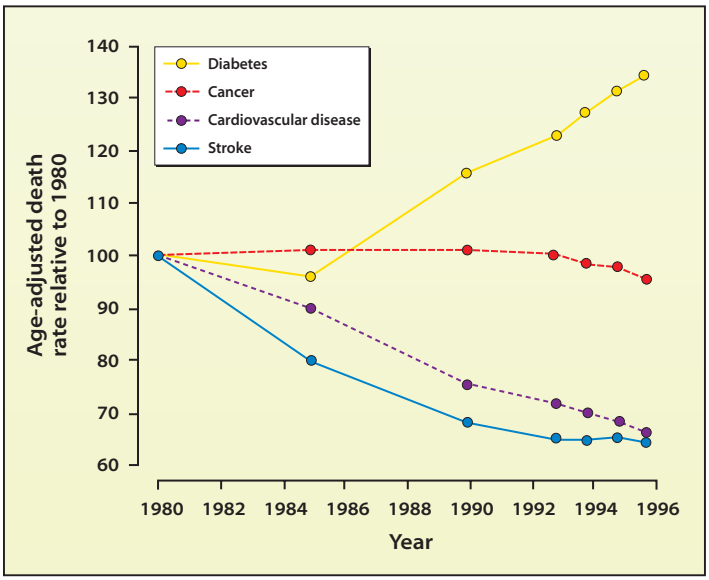

Figure 1. *Survival curves for diabetes, cancer, cardiovascular disease, and stroke. Data are derived from the National Center for Health Statistics. Adapted with permission from McKinlay and Marceau.*[5]

middle-aged adults, the elderly,[3] and, unexpectedly, among children. Although the underpinnings of these epidemiologic observations have yet to be fully realized, there has been a parallel increase in the prevalence of societal obesity.[4] Unfortunately, cardiovascular complications remain the leading cause of death among patients with type 2 DM, accounting for 70% of all case-fatalities. Although there has been a recent decline in the age-adjusted mortality rate among patients with cardiovascular disease, there has not been a coincident reduction in the adjusted mortality rates among patients with diabetes[5,6] (Figure 1). Data from several studies have compelled numerous expert panels, including the Joint National Committee (JNC) VI, American Diabetes Association (ADA), and the National Cholesterol Education Program (NCEP), to recommend an aggressive risk-factor modification program, with a reduction in traditional risk factors and the early addition of oral antiplatelet therapy.

Insulin Resistance

Insulin resistance precedes the onset of overt hyperglycemia in approximately 80% of patients[7] and is a known cardiovascular risk factor. Although the biological determinants of insulin resistance are varied and remain mostly unexplained, emerging mechanisms have been implicated in its pathophysiology. The insulin receptor gene is located on chromosome 19, and there have been no fewer than 50 mutations in this gene described, which, taken in total, cause only rare forms of insulin resistance. However, insulin resistance appears, in part, to be genetically determined. Young, non-obese and glucose-tolerant relatives of patients with type 2 DM have demonstrated insulin resistance.[8,9] The genetic drivers of insulin resistance do not appear to be absolute, because environmental factors clearly contribute to the development of diabetes. Although the molecular underpinnings of insulin resistance have not yet been defined, numerous agents have been implicated and are discussed in detail below.

The recently updated NCEP guidelines recognize insulin resistance as an important and modifiable cardiovascular risk factor. Insulin resistance, as determined by this expert panel, is present when any 3 of the following exist in a given patient: a fasting glucose of > 110 mg/dL, elevated triglycerides (≥ 150 mg/dL), central adiposity (abdominal girth > 102 cm in men and > 88 cm in women), hypertension (≥ 130/≥ 85 mm Hg), and depressed high-density lipoprotein (HDL) (< 40 mg/dL in men and < 50 mg/dL in women) (Table 1). Insulin resistance has been linked to increased production of proinflammatory cytokines and ultimately to the development of both type 2 DM and atherosclerosis.[10–12]

In addition to diet and exercise, modulation of insulin resistance is currently possible with both metformin and the thiazolidinediones (TZDs). There are currently 2 TZD agents commercially available in the United States: rosiglitazone and pioglitazone. Troglitazone was voluntarily withdrawn from the market in March 2000, owing to unexpected, severe hepatotoxicity. The glucose-lowering effects of TZDs have been extensively studied in humans. It appears that, as a class, they improve

Table 1
Clinical Correlates of Insulin Resistance (National Cholesterol Education Program III)

Any 3 of the Following:
Fasting glucose ≥ 110 mg/dL
Triglycerides ≥ 150 mg/dL
High-density lipoprotein Male: < 40 mg/dL Female: < 50 mg/dL
Waist circumference Male: > 102 cm Female: > 88 cm
Hypertension (≥ 130/≥ 85 mm Hg)

glycemic control somewhat less than the sulfonylurea agents or metformin. On average, the fasting plasma glucose level is decreased by approximately 45 mg/dL and hemoglobin (Hb)A_{1c} by approximately 1%.[13,14] The glucose-lowering effects of these agents appear to plateau at doses greater than 8 mg for rosiglitazone and 45 mg for pioglitazone.

TZDs also have numerous non–glucose-lowering effects that are potentially advantageous. They have a favorable impact on lipoprotein metabolism, fibrinolysis,[15] endothelial function, and inflammation. As a general rule, TZD agents increase HDL levels as much as 20% and decrease triglyceride levels, especially when these levels are markedly elevated, as is often the case with type 2 DM patients. Although TZD agents minimally elevate total low-density lipoprotein (LDL) concentration, they transition small, oxidized LDL particles to larger, buoyant, potentially less atherogenic particles.[16] Troglitazone administration has also been demonstrated to result in significant regression of carotid intimal medial wall thickness.[17]

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TZDs can, however, be associated with potentially serious adverse effects, such as the development of fluid retention and worsening congestive heart failure symptoms. Thus, these agents are contraindicated in patients with New York Heart Association III–IV symptoms. Preclinical studies in a murine model for familial adenomatous polyposis and sporadic colon carcinoma suggested that activation of peroxisome proliferation-activated receptor γ was tumor-producing. Thus, TZDs should not be prescribed to persons with familial adenomatous polyposis coli.[18,19]

Hypertension, Renin–Angiotensin Axis, and Diabetes Mellitus

Hypertension remains a prevalent and readily modifiable chronic disease. Approximately 11 million Americans have both diabetes and hypertension. This "deadly duo" increases cardiovascular event rates 2-fold. Furthermore, hypertension among diabetic patients has been linked with numerous other vascular complications, such as nephropathy, retinopathy, cerebrovascular disease, and significant decline in cognitive function, in middle-aged patients.[20]

Recognizing this link between hypertension and diabetes and adverse events, numerous expert panels have recommended lower blood pressure targets for patients with diabetes mellitus.[21–23] Before substantial efficacy data became available, the JNC VI recommended a reduction of the target blood pressure among diabetic patients to 130/85 mm Hg.[23] The ADA currently recommends a targeted blood pressure of 130/80 mm Hg. This later recommendation has now been validated in 2 large-scale clinical trials. Both the Hypertension Optimal Treatment (HOT) trial[24] and the UK Prospective Diabetes Study 38[25] implemented a multidrug antihypertension regimen, achieved a targeted low blood pressure, and demonstrated improved outcomes among the intensively managed diabetic patients. Based on the HOT trial findings, there were an additional 7.4 lives saved per 1000 patient-years treated in the ≤ 80 mm Hg group. Adopting either of these guidelines not only seems efficacious but is also likely to translate into an estimated lifetime cost savings of $1450.[26]

Numerous pharmacologic agents have been investigated for the treatment of hypertension among diabetic patients; however, angiotensin-converting enzyme (ACE) inhibitors should be considered first-line agents. Their efficacy was initially established for diabetic patients with acute myocardial infarction (MI),[27] with nephropathy,[25,28–31] and in the presence of congestive heart failure. Both the ABCD trial and the Fosinopril Versus Amlodipine Cardiovascular Events Randomized Trial (FACET)[30] randomized type 2 DM patients to either an ACE inhibitor or calcium antagonist, and both demonstrated a reduction in cardiovascular events for patients randomized to ACE inhibition therapy. FACET randomized patients with diabetes and hypertension to fosinopril or amlodipine. Despite a similar reduction in diastolic blood pressure among both agents, fosinopril treatment was associated with a 50% reduction in acute MI, stroke, or angina requiring hospitalization. Although not the primary focus of this trial, these results highlight the importance of ACE inhibition

The ADA currently recommends a targeted blood pressure of 130/80 mm Hg.

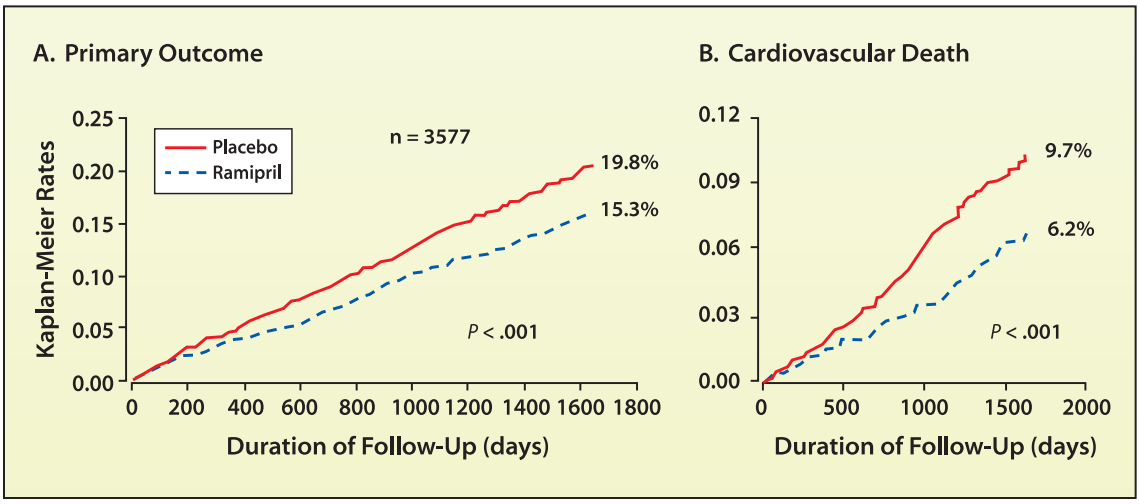

Figure 2. *Kaplan-Meier estimates for all-cause mortality for diabetic patients enrolled in the Microalbuminuria, Cardiovascular, and Renal Outcomes in the Heart Outcomes Prevention Evaluation (MICRO-HOPE) study. Reproduced with permission from the Heart Outcomes Prevention Evaluation Study Investigators.*[32]

among diabetic patients.[30]

Further extending the efficacy and indications of ACE inhibition among patients with diabetes are the Microalbuminuria, Cardiovascular, and Renal Outcomes in the Heart Outcomes Prevention Evaluation (MICRO-HOPE) data.[32] In this trial, 3577 patients with a history of diabetes and cardiovascular disease or 1 other risk factor for heart disease were eligible for randomization.[33] There was a 25% reduction in MI, stroke, or cardiovascular death for the ramipril-treated diabetic cohort ($P = .0004$) (Figure 2A). The mortality rate was 9.7% for the placebo-treated patients, compared with 6.2% for the ramipril-treated patients ($P < .001$) (Figure 2B). There was also a significant reduction in the rate of MI (12.9% vs 10.2%, $P = .01$) and stroke (6.1% vs 4.2%, $P = .007$) for the ramipril-treated diabetic patients compared with nondiabetic patients.

Although angiotensin receptor blockers (ARBs) have emerged as effective agents in treating hypertension and in preventing the progression of nephropathy among patients with type 2 DM, they should be considered for use only among patients intolerant of or allergic to ACE inhibition, given the current breadth of data for ACE inhibitors. ARBs might offer more comprehensive inhibition of the renin–angiotensin system via inhibition of the angiotensin II tissue receptor, a reduced incidence of hyperkalemia, and no increased incidence of chronic cough associated with long-term usage.[34]

The results of 4 large-scale trials confirmed earlier pilot studies suggesting beneficial renal effects of ARBs (Table 2).[35–37] The Reduction of Endpoints in Non Insulin Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan (RENAAL) trial and the Irbesartan Diabetic Nephropathy Trial (IDNT) evaluated the efficacy of losartan and irbesartan among patients with type 2 DM with proteinuria and elevated creatinine. Both trials demonstrated a significant reduction in the rate of death, development of end-stage renal disease, or doubling of serum creatinine levels. The primary composite endpoint was 43.5% for the losartan-treated group, compared with 47.1% for the placebo-treated group ($P = .024$) in the RENAAL trial.[36,38]

The IRbesartan in Type 2 Diabetes with MicroAlbuminuria (IRMA II) and MicroAlbuminuria Reduction With VALsartan (MARVAL) trials randomized patients with type 2 DM, microalbuminuria, and normal creatinine levels to either irbesartan versus placebo or valsartan versus amlodipine, respectively. The primary endpoint in these smaller, controlled trials was the development of frank proteinuria. Both of these trials demonstrated significant reduction in the development of proteinuria with ARBs. In the MARVAL trial, 29.9% of valsartan-treated patients returned to normal albuminuric states, compared with 14.5% of the amlodipine-treated patients ($P = .001$.).[36,39]

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The safety, tolerability, and efficacy of ß-blockers among patients with type 2 DM have been established.[40,41] In a large series of diabetic patients with acute MI, there was an approx-

Table 2
Clinical Trials Evaluating the Efficacy of Angiotensin Receptor Blockers in Type 2 Diabetes*

	N	Agents	Clinical Setting	Primary End Point	↓ Relative Risk	*P*
RENAAL	1513	Losartan Placebo	Type 2 DM, proteinuria and increased creatinine, 94% of patients also had HTN	Composite: Death, ESRD, or doubling creatinine	16%	.024
IDNT	1715	Irbesartan Amlodipine Placebo	HTN, type 2 DM, proteinuria > 900 mg/dL	Death, ESRD, or doubling creatinine	33%	< .05
IRMA II	590	Irbesartan Placebo	Type 2 DM, normal creatinine and microalbuminuria, UAER 20–200 μg/min	UAER > 200 μg/min and > 30% from baseline	70%	.0004
MARVAL	332	Valsartan Amlodipine	Type 2 DM, microalbuminuria	UAER (mean)	n/a	< .001

RENAAL, Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan; IDNT, Irbesartan Diabetic Nephropathy Trial; IRMA II, IRbesartan in Type 2 Diabetes with MicroAlbuminuria; MARVAL, MicroAlbuminuria Reduction With VALsartan; DM, diabetes mellitus; HTN, hypertension; UAER, urinary albumin excretion rate; ESRD, end-stage renal disease.
* Presented at the American Society of Hypertension 16th Annual Scientific Sessions.

imately 40% reduction in mortality among patients receiving ß-blockers.[41] The 2-year mortality rate was 17% for patients treated with a ß-blocker, compared with 26.6% for patients not receiving a ß-blocker (relative risk 0.64; 95% confidence limits 0.60-0.69). Unfortunately, in this large analysis, only 31% of eligible diabetic patients received treatment with a ß-blocker after infarction.

Efficacy of ß-blocker therapy is also evidenced in a study of diabetic patients with known stable coronary artery disease within the Bezafibrate Infarction Prevention trial.[42] Within this study, there was a 44% reduction in the 3-year mortality rates for diabetic patients receiving ß-blockers.

Treatment with ß-adrenergic antagonists is associated with insulin resistance and impaired lipid metabolism. Unlike selective ß-blockers, carvedilol is a nonselective ß adrenoreceptor and selective ß adrenoreceptor-blocking agent. Its ratio of ß to α blocking potency is 7.6 to 1. In a small, prospective, randomized, controlled trial of patients with type 2 DM, the efficacy of carvedilol was compared with atenolol.[43] Blood pressure and left ventricular mass decreased in both treatment groups; however, carvedilol use was associated with a significant reduction in fasting plasma glucose, insulin, and triglyceride levels, as well as with an increase in HDL cholesterol, compared with atenolol. Carvedilol and atenolol are currently being evaluated in a large, randomized trial.

Dyslipidemia and Diabetes

Patients with type 2 DM have a characteristic lipoprotein profile, including a tendency for hypertriglyceridemia, low levels of HDL cholesterol, and modestly elevated LDL cholesterol, with a disproportionately elevated level of small-oxidized LDL particles. Both the Scandinavian Simvastatin Survival Study (4S) and the Cholesterol and Recurrent Events (CARE) study have demonstrated a significant reduction in future cardiovascular end points for patients with diabetes and coronary heart disease treated with hydroxymethylglutaryl coenzyme A (HMG CoA) reductase inhibitor.[44,45]

A primary prevention strategy is currently being tested in the Atorvastatin Study in Preventing Endpoints in NIDDM (ASPEN) study and was recently tested in the Collaborative Atorvastatin Diabetes Study (CARDS). CARDS demonstrated a significant reduction in primary endpoints, including death, nonfatal MI, and stroke, among lower-risk diabetic patients randomized to atorvastatin (5.8% vs 9%, $P = .001$), as well as a 36% reduction in acute coronary events, a 31% reduction in coronary revascularization, and a 48% reduction in stroke. Results were consistent regardless of baseline lipid levels.

Adjunctive Oral Antiplatelet Therapy

Numerous plausible biological mechanisms have been purported to explain the exceptionally poor outcome of patients with diabetes mel-

litus and coronary artery disease. Diabetic patients have a propensity for adverse arterial remodeling,[46,47] aggressive atherosclerosis,[48,49] abnormal endothelial function,[50,51] impaired fibrinolysis, platelet hyperactivity, and a propensity to form neointima after arterial injury.

The diabetic platelet has emerged as a distinct target for therapeutic intervention. Increased platelet activity is certainly involved in the increased thrombogenic potential among diabetic patients. Diabetic platelets are larger, have a greater number of glycoprotein (GP) IIb/IIIa receptors,[52] and aggregate more readily to known agonists in vitro than nondiabetic platelets.[53] Furthermore, a greater percentage of diabetic platelets circulate in an activated state. Knobler and associates[54] measured shear-induced whole-blood platelet adhesion and aggregation on the extracellular matrix of diabetic and nondiabetic patients. This study demonstrated increased platelet adhesion and aggregation in diabetic patients, which loosely correlated with the degree of dyslipidemia.

It is not surprising that diabetic patients derive substantial benefit from aspirin therapy. A meta-analysis from the Anti-Platelet Trialists evaluated the efficacy of aspirin therapy as a secondary preventive strategy. The diabetic substudy in this meta-analysis demonstrated a significant reduction in cardiovascular events for diabetic patients treated with aspirin, with an estimated 38 vascular events prevented per 1000 diabetic patients treated.[55] Subgroup analysis from the U.S. Physician's Health Study evaluated the efficacy of low-dose aspirin (325 mg qod) as a primary prevention strategy.[56] Subgroup analysis of this diabetic cohort demonstrated a reduction in the MI rate, from 10.2% for the placebo-treated group to 4.0% for the aspirin-treated group. Given these historical data, aspirin administration is requisite among diabetic patients with coronary heart disease and seems prudent in patients with type 2 DM at risk for coronary heart disease.

Treatment with a thienopyridine might confer additional benefit among diabetic patients with macrovascular disease. The Clopidogrel vs Aspirin in Patients at Risk of Ischemic Events (CAPRIE) trial randomized 19,185 patients with a history of recent stroke, MI, or peripheral arterial disease to either aspirin or clopidogrel. Overall, there was a modest reduction in the combined event rates of ischemic stroke, MI, or vascular death associated with clopidogrel treatment compared with aspirin therapy (5.83% vs 5.32%, respectively, $P = .043$). Substudy analysis of the nearly 4000 diabetic patients from CAPRIE, randomized to clopidogrel, demonstrated a significant benefit.[57] The annual combined event rate was 17.7% compared with 15.6% ($P = .042$).

Table 3
Order of Priorities for Treatment of Diabetic Dyslipidemia in Adults

I. LDL cholesterol lowering

First choice

HMG CoA reductase inhibitor (statin)

Second choice

Ezetimibe, bile acid binding resin (resin), or fenofibrate

II. HDL cholesterol raising

- Behavioral interventions, such as weight loss, increased physical activity, and smoking cessation may be useful
- Glycemic control
- Difficult except with nicotinic acid, which is relatively contraindicated, or fibrates

III. Triglyceride lowering

- Glycemic control first priority
- Fibric acid derivative (gemfibrozil, fenofibrate)
- Statins are moderately effective at high dose in hypertriglyceridemic subjects who also have high LDL cholesterol

IV. Combined hyperlipidemia

First choice

Improved glycemic control plus high-dose statin

Second choice

Improved glycemic control plus high-dose statin plus fibric acid derivative (gemfibrozil, fenofibrate)

Third choice

Improved glycemic control plus resin plus fibric acid derivative (gemfibrozil, fenofibrate)

Improved glycemic control plus statin plus nicotinic acid (glycemic control must be monitored carefully)

LDL, low-density lipoprotein; HDL, high-density lipoprotein; HMG CoA, hydroxymethylglutaryl coenzyme A.

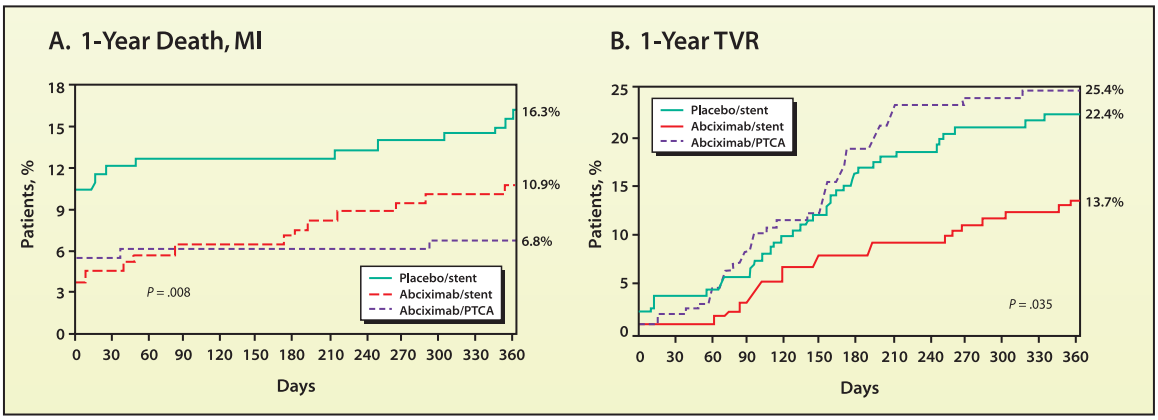

Figure 3. *One-year Kaplan-Meier estimates of the invasive treatment arms for the patients with diabetes mellitus enrolled in the Evaluation of Platelet IIb/IIIa Inhibition for Stenting (EPISTENT) trial.* **(A)** *Rate of death or myocardial infarction (MI) within EPISTENT.* **(B)** *One-year target vessel revascularization (TVR) rates. PTCA, percutaneous transluminal coronary angioplasty.*

Adjunctive Therapy During Percutaneous Coronary Intervention

Diabetic patients undergoing percutaneous coronary intervention (PCI) have numerous high-risk clinical and anatomic characteristics and substantially higher rates of late MI, late mortality, and restenosis after PCI. Recent data analyzing more than 25,000 patients undergoing PCI suggest that diabetic patients also have an approximately 2-fold increase in in-hospital mortality after both elective (1% vs 2%, $P < .001$) and urgent (6.9% vs 12.7%, $P < .001$) PCI. This increased early hazard for death after PCI persisted after multivariate adjustment (odds ratio 1.4, $P = .04$).[58] In addition to aspirin and a thienopyridine, the adjunctive administration of a GP IIb/IIIa inhibitor has been associated with an additional reduction in adverse events after PCI.

The early safety and long-term efficacy of abciximab has been extensively evaluated among patients with diabetes undergoing PCI. Of the 2399 patients randomized within the Evaluation of Platelet IIb/IIIa Inhibitor for Stenting (EPISTENT) trial, 491 patients had a history of diabetes mellitus and were randomized to stent–abciximab (SA), stent–placebo (SP), or percutaneous transluminal coronary angioplasty (PTCA)–abciximab (BA).[59] The benefit of abciximab therapy among diabetic patients undergoing PCI was apparent at 30 days, persisted through 1-year follow-up, and remained significant after multivariate adjustment. At 6 months, there was a marked benefit for the SA group compared with the SP and the BA groups for the combined end point of death, MI, or target vessel revascularization (SA 13.0%, SP 25.2%, $P < .005$; BA 23.4%). The reduction in this composite was driven by a reduction in all 3 end points analyzed. The 6-month death or MI rates were 6.2% for the SA, 12.7% for the SP ($P = .041$), and 7.8% for the BA groups. There was also a significant reduction in the 6-month target vessel revascularization rate for diabetic patients treated with stent and abciximab (SA 8.1%, SP 16.6%, $P = .021$; BA 18.4%). Importantly, the efficacy of stent and abciximab was maintained through 1-year follow-up (Figure 3).

The initial findings from EPISTENT have been further substantiated by a pooled analysis from the EPIC (Evaluation of IIb/IIIa Platelet receptor antagonist 7E3 in Preventing Ischemic Complications), EPILOG (Evaluation of PTCA to Improve Long-term Outcome by c7E3 GPIIb/IIIa receptor blockade), and EPISTENT trials.[60] The administration of abciximab was associated with a significant reduction in 1-year mortality among the 1462 diabetic patients in these trials (4.5% vs 2.5%, $P = .031$). The efficacy of abciximab persisted among high-risk subgroups of diabetic patients, including those with clinical markers of insulin resistance (5.1%, 2.3%, $P = .0044$), insulin-requiring diabetic patients (8.1% vs 4.2%, $P = .073$), and those diabetic patients undergoing multivessel intervention (7.7% vs 0.9%, $P = .018$).

Summary

There remains no doubt that patients with type 2 DM remain at heightened risk for major cardiovascular events in the modern era of medical therapy. It is also clear that this group of patients derives substantial benefit from current recommendations regarding risk factor modification and available pharmacologic agents. Unfortunately, attaining the recommended risk factor targets and instituting a broad-based pharmacologic treatment strategy has been less than successful.[61] Improving cardiovascular health among patients with diabetes will require an increase of societal resources. Focused and effective prevention strategies that are readily applicable across cultures will be essential for delaying, and ultimately

preventing, the onset of type 2 DM. The medical community needs to become engaged with respect to the unique nature of diabetes mellitus and vascular disease and implement broad-based treatment strategies resulting in "poly-pharmacy" of the diabetic person. A reinvestment of philanthropy, industry, and government-based research resources will be required to propel our current understanding of the diabetic–vascular axis forward. ■

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Main Points

- Cardiovascular complications are the leading cause of death among patients with type 2 diabetes mellitus (DM), accounting for 70% of all case-fatalities. Although there has been a recent decline in the age-adjusted mortality rate among patients with cardiovascular disease, there has not been a coincident reduction in the adjusted mortality rates among patients with diabetes.
- The recently updated National Cholesterol Education Program guidelines recognize insulin resistance as an important and modifiable cardiovascular risk factor. In addition to diet and exercise, modulation of insulin resistance is currently possible with both metformin and the thiazolidinediones.
- Thiazolidinediones also have numerous non–glucose-lowering effects that are potentially advantageous; however, they can be associated with potentially serious adverse effects, such as the development of fluid retention and worsening congestive heart failure symptoms.
- Because of the link between combined hypertension and diabetes and adverse events, numerous expert panels have recommended lower blood pressure targets for patients with diabetes mellitus. Angiotensin-converting enzyme (ACE) inhibitors should be considered first-line agents for the treatment of hypertension among diabetic patients.
- Although angiotensin receptor blockers have emerged as effective agents in treating hypertension and in preventing the progression of nephropathy among patients with type 2 DM, they should be considered for use only among patients intolerant of or allergic to ACE inhibition.
- Given the historical data, aspirin administration is requisite among diabetic patients with coronary heart disease and seems prudent in patients with type 2 DM at risk for coronary heart disease.
- Diabetic patients undergoing percutaneous coronary intervention (PCI) have numerous high-risk clinical and anatomic characteristics and substantially higher rates of late myocardial infarction, late mortality, and restenosis after PCI. The administration of abciximab has been associated with a significant reduction in 1-year mortality among diabetic patients.

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