

NEWS FROM THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS (AAACE) 17TH ANNUAL MEETING AND CLINICAL CONGRESS
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ORLANDO, FLA

Vitamin D Deficiency: A Near-Universal Health Problem

“Vitamin D deficiency is a tremendously important public health problem,” according to Robert P. Heaney, MD, FACP, FACN, of the Creighton University Osteoporosis Research Center, “and until we can rectify the epidemic of vitamin D deficiency, I do not think we really know what the burden of chronic disease really is.”

During an AAACE workshop, Dr. Heaney said that vitamin D is an integral component of the mechanism whereby cells control gene transcription in response to a variety of stimuli. Adequate vitamin D status enables optimal response to a broad variety of signals. More than 100 years ago, physicians recognized that severe vitamin D deficiency was expressed as rickets in children and osteomalacia in adults. Until recently, however, there was no way of assessing lesser degrees of vitamin D deficiency. Now that a good blood test exists, physicians realize that most individuals have deficient vitamin D levels.

A variety of studies in the United States and Europe have shown that anywhere from 65% to 100% of a given population will be low or at the bottom range of normal for vitamin D levels—that qualifies as a near-universal problem.

Strong evidence exists that several chronic disorders are associated with lesser degrees of vitamin D deficiency, such as type 1 diabetes, hypertension, cardiovascular disease (CVD) in general, falls, neuromuscular function, and even cancer. “The consequences of this near-universal disorder is that it contributes to the burden of disease that afflicts the population at the end of life.”

What Do We Really Know About the Pathogenesis and Natural History of Type 1 Diabetes?

It was once thought that type 1 diabetes was caused by a virus and that it developed very quickly, according to Mark Atkinson, PhD, of the University of Florida. Since that time, a lot has been learned about how type 1 diabetes develops. Dr. Atkinson spoke during an AAACE general session.

“There are many clinical trials looking at reversing the disease,” he said. “One of the major things that needs to happen is a breakthrough in finding out what in the environment has changed to cause marked increases in childhood diseases. The second thing that will help in terms of finding a cure is continued collaborative research efforts that involve getting more endocrinologists and pediatricians to participate in clinical trials.”

Autoimmunity underlies the development of type 1 diabetes, and there is a complex interaction between genetics

and the environment. In primary prevention, the goal is to prevent autoantibody production that causes the development of overt disease. Dietary approaches are being looked at as well as antigen-specific therapy, insulins, and proinsulins. In secondary prevention, the goal is to induce remission and preserve C-peptide. TrialNet is an international clinical trials network, the goal of which is to explore new therapies and further define the epidemiology, natural history, and risk factors for type 1 diabetes. For more information, visit www2.diabetestrialnet.org.

CGM Use as an Indicator of the Metabolic Effects of Islet Transplantation

Lisa Gorn, DO, of the Diabetes Research Institute at the University of Miami, and colleagues, reported that a continuous glucose monitor (CGM) was useful for assessing metabolic control among patients with type 1 diabetes who had undergone islet transplantation (Abstract 225).

The investigators also wanted to see if a CGM could be an indicator of dysfunction. They followed 12 patients with type 1 diabetes who had undergone islet transplantation and used a CGM at 3-month intervals, up to 18 months after they were transplanted, to assess metabolic control, and compared them with 13 control patients.

“We found that patients who had islet transplantation had significantly fewer episodes of hypoglycemia throughout the study period, spent more time in normoglycemia, and had improved glycemic control and metabolic stability compared with control patients.” She said that the CGM was useful in telling investigators how well patients were doing after transplantation, and it also indicated when patients were not doing well.

“We hope that with the use of a real-time CGM we can better predict graft dysfunction allowing earlier intervention,” Dr. Gorn said. New clinical islet transplantation studies are underway, which can provide new methods to improve transplantation results, she added.

Resveratrol’s Effect on Glut-1 Mediated Transport

Numerous studies have indicated that resveratrol, a component in red wine, has cardioprotective, antiviral, and anticancer properties. More recently, it has been suggested that the agent also has antidiabetic properties and that it may reduce blood glucose levels in animals.

Kimberly Martin, MD, a pediatric endocrinology fellow at Case Western Reserve University, Cleveland, reported on how resveratrol affects the glucose transporter-1 (GLUT-1), which is found in virtually all tissue. When resveratrol was added to Clone 9 cells (a rat liver cell line expressing only the GLUT-1 isoform), it was found to lower glucose transport to almost complete inhibition (Abstract 229).

“We also went on to see how resveratrol was acting on the cell, and it appears that it is binding directly to the cell to inhibit glucose transport. This is a potential medication that could be used in multiple areas,” she said. The work to date

has been in cell culture and not in animals, which is the future direction of the work.

Dr. Martin added that, although resveratrol is a component of red wine, one would have to drink 10 to 100 bottles of red wine to have doses equivalent to any of the studies that have been done.

Osteoporosis: What's New and What's Next?

Osteoporosis is a serious and expensive public health problem that is underdiagnosed and undertreated, according to Nelson Watts, MD, FACP, MACE, of the University of Cincinnati's Bone Health and Osteoporosis Center. During an ACE general session, he said that Medicare cuts in dual energy x-ray absorptiometry, or DXA, will create access problems for women, which will only intensify the problem.

New 2008 National Osteoporosis Foundation guidelines (available at www.nof.org) for treatment will more appropriately focus treatment on patients who will have an increased benefit in the near term, he said. There is still an issue with older patients who have fractured or know they are likely to fracture, not being identified and treated.

Toward this end, the FRAX tool (available at www.shef.ac.uk/FRAX/) has been developed by the World Health Organization to evaluate the fracture risk of patients. It is based on individual patient models that integrate the risks associated with clinical risk factors as well as bone mineral density at the femoral neck.

There is new information about existing treatments and new treatment options—such as the yearly intravenous bisphosphonate injection—and new understandings in bone biology that should lead to better treatments in the future that more specifically target sites in bone remodeling that can make bone stronger, and patients can live longer and better, Dr. Watts added.

NEWS FROM THE AMERICAN DIABETES ASSOCIATION (ADA) 68TH SCIENTIFIC SESSIONS

JUNE 6–10, 2008
SAN FRANCISCO

Translating A1C Into Estimated Average Glucose

A mathematical relationship between the average glucose level over the preceding three months and levels of the A1C test, thus yielding translation of the A1C for reporting as estimated average glucose (eAG), was proven in an international study. These results were presented at the ADA meeting and published simultaneously online in *Diabetes Care*.

Speaking at a news conference, David M. Nathan, MD, Professor of Medicine, Harvard Medical School, and Cochair of the ADAG (International A1C-Derived Average Glucose) Study said that A1C has been used for more than 25 years as the major measure of glucose control and to establish targets for diabetes therapy.

"The findings of this large study have confirmed what

smaller studies have shown and will give us confidence that A1C really does represent an average glucose because we now have a reliable formula to convert A1C into average glucose," said Dr. Nathan. "While eAG will not replace A1C, physicians will be able to obtain reports both in A1C units of glycated hemoglobin and eAG units of milligrams per deciliter or millimols per liter, depending on the country, and choose which to use in clinical situations."

ADAG Cochair, Robert J. Heine, MD, PhD, Professor of Diabetology in the Department of Endocrinology at the VU University Medical Center in Amsterdam, Netherlands, and Executive Medical Director of the Diabetes and Endocrine Division of Eli Lilly and Company, said: "It is extremely helpful for health care professionals and patients to be using the same language to discuss glucose goals. As patients sometimes find it difficult to understand the concept of glycated hemoglobin, it will be much easier to have all test results—both those from the lab and those the patient performs—in the same units."

With A1C translated from a difficult-to-understand chemical entity into an easy-to-understand value that relates to the patient's everyday home glucose monitoring, Dr. Heine predicts that eAG will prove to be a valuable education tool.

The ADA, European Association for the Study of Diabetes (EASD), and International Diabetes Federation (IDF) will be working together to conduct educational efforts to make both patients and providers aware of this new terminology, and help to understand the relationship between A1C and eAG. Physicians can visit the ADA Web site at www.diabetes.org to purchase an inexpensive handheld calculator that will provide an instant conversion of A1C values to eAG.

Health Care Providers Urged to Address Type 2 Diabetes, Sleep Apnea Link

Research demonstrates that type 2 diabetes and obstructive sleep apnea (OSA) are closely related and both disorders have significant implications on individuals and public health. These findings have led to an IDF task force statement that was released here at during a joint IDF/ADA symposium and simultaneously posted online in *Diabetes Research and Clinical Practice*.

"While type 2 diabetes is recognized as a serious global epidemic, the severe health consequences of untreated [OSA], especially in people with diabetes, are not. Health policymakers and the general public must be made aware of the link between type 2 diabetes and [OSA] so that we can begin to address the significant economic burden and debilitating health consequences to both individuals and the community," said Prof. Paul Zimmet, Foundation Director of the International Diabetes Institute in Melbourne, Australia and Cochair of the IDF Task Force on Epidemiology and Prevention. "Today's statement is an urgent call to action to the medical community. It is impera-

tive that we better understand the relationship between diabetes and [OSA] through research and establish appropriate standards of care for managing diabetes and comorbidities such as [OSA].”

Recent studies show that OSA is common in people with diabetes: Estimates suggest that up to 40% of people with OSA have diabetes. Further research is needed in this area in order to strengthen the evidence base between diabetes and OSA, according to an IDF news release.

Both conditions have tremendous economic implications: The annual costs of diabetes alone amount to \$170 billion in the United States. Prof. Zimmet said the estimated annual medical costs of OSA are much harder to define.

It has also been shown that the prevalence of CVD increases progressively with the increasing severity of OSA and that people with diabetes and/or OSA face serious cardiovascular problems and earlier death. Undiagnosed OSA may interfere with lifestyle treatment for diabetes. The IDF strongly recommends that health care professionals working in both type 2 diabetes and sleep disorders are educated about the links between the two conditions and encouraged to adopt clinical practices to ensure that a person presenting with one condition is considered for the other.

Periodontitis Associated With Development of Type 2 Diabetes, Complications

Critical links between periodontal disease and the development of type 2 diabetes, as well as the development and progression of its complications, were reported at the ADA in the first-ever symposium presented by dentists to diabetes experts.

“One of the many complications of diabetes is a greater risk for periodontal disease,” said Maria E. Ryan, DDS, PhD, Professor of Oral Biology and Pathology, and Director of Clinical Research, School of Dental Medicine, Stony Brook University, NY, in a news release. “If you have this oral infection and inflammation, as with any infection, it’s much more difficult to control blood glucose levels.” Intensive periodontitis treatment significantly reduces levels of A1C.

The links between oral and systemic health may start even before clinical diabetes begins. “We have found evidence that the severity of periodontal disease is associated with higher levels of insulin resistance, often a precursor of type 2 diabetes, as well as with higher levels of A1C, a measure of poor glycemic control of diabetes,” Dr. Ryan said.

The importance of these findings were emphasized by George W. Taylor, DrPH, DMD, Associate Professor of Dentistry, Schools of Dentistry and Public Health, University of Michigan. “Several recent studies have shown that having periodontal disease makes those with type 2 diabetes more likely to develop worsened glycemic control and puts them at much greater risk of end-stage kidney disease and death,” he reported. “Given the numerous medical studies showing that good glycemic control results in reduced development

and progression of diabetes complications, we believe there is the potential that periodontal treatment can provide an increment in diabetes control and subsequently a reduction in the risk for diabetes complications,” said Dr. Taylor.

Sustained Improvements in Glycemic Control and Weight Seen With Exenatide Once Weekly

Results from a 52-week open-label clinical study showed the durable efficacy of exenatide once weekly, a long-acting release formulation of exenatide (Abstract 107-OR). Patients taking exenatide (Byetta, Amylin Pharmaceuticals, Inc. and Eli Lilly and Company) once weekly for 1 year sustained a similar improvement in glucose control (A1C: $-2.0\% \pm 0.08$; fasting plasma glucose: -47 ± 3 mg/dL) versus those receiving treatment for 30 weeks (A1C change from baseline: $-1.9\% \pm 0.08$).

This study also showed that patients who switched from exenatide injection after 30 weeks to exenatide once weekly experienced additional improvements in A1C and fasting plasma glucose, according to a news release. Seventy-four percent of all patients in the study achieved an endpoint A1C of $\leq 7\%$ or less at 52 weeks. Patients in both treatment groups experienced a statistically significant and sustained average weight loss of 9.5 lbs over 52 weeks.

Exenatide is indicated as adjunctive therapy to improve glycemic control in patients with type 2 diabetes who are taking metformin, a sulfonylurea, a thiazolidinedione, a combination of metformin and a sulfonylurea, or a combination of metformin and a thiazolidinedione but have not achieved adequate glycemic control.

“Diabetes is a lifelong condition that requires constant management of blood glucose or blood sugar as well as weight. In the DURATION-1 trial, patients reduced their blood glucose levels and, on average, lost a total of >9 lbs. These improvements were sustained for 1 year,” said John B. Buse, MD, PhD, Professor of Medicine, Director of the Diabetes Care Center, and Chief of the Division of Endocrinology at the University of North Carolina School of Medicine. “Importantly, the study results also showed that steady-state levels of exenatide may result in improvements in a variety of glucose parameters. If approved, exenatide once weekly may provide patients with a treatment option that is on board 24 hours a day, 7 days a week, helping to manage their blood sugar and, secondarily, their weight.”

Safety and Efficacy of ISIS 388626, an Optimized SGLT2 Antisense Inhibitor

Preclinical data show that antisense drugs potentially reduce levels of sodium-dependent glucose cotransporter type 2 (SGLT2), a key component in controlling glucose reabsorption in the kidney and the target of ISIS 388626 (Isis Pharmaceuticals), according to a company news release. Antisense reduction of SGLT2 produced the following results in preclinical models (Abstract 3304-OR):

- Lowered A1C over time in diabetic animals and reduced postprandial and fasting blood glucose levels while also ameliorating diabetic complications, including slowing progression of cataract formation;

- Lowered SGLT2 mRNA levels in the kidney by approximately 80% in all species tested, with doses as low as 1 to 2 mg/kg/week with no effect on SGLT1, a related protein, where levels of activity are desirable; and

- Showed no changes in urinary or plasma markers of renal function and no harmful effects such as low blood glucose.

“In preclinical models, lowering levels of SGLT2 in the kidney by an antisense drug demonstrated very potent reduction in blood glucose that supports the possibility of an infrequent monthly injectable dosing or, potentially, a cost-effective oral administration. Furthermore, our SGLT2 inhibitor complements our diabetes drugs in development and offers a unique and complementary approach to treat diabetes,” said Sanjay Bhanot, MD, PhD, Vice President of Metabolic Diseases Research & Development of Isis Pharmaceuticals.

“We are moving ISIS 388626, our human antisense SGLT2 inhibitor, toward human clinical proof-of-concept as rapidly as possible, and we look forward to continuing to populate our metabolic disease pipeline with exciting drugs arising from our research program,” Dr. Bhanot said.

Lantus Helped Type 2 Diabetes Patients Achieve ADA Goal

Results from a new study presented here reinforce the importance of promptly initiating insulin treatment when patients with type 2 diabetes are unable to achieve recommended glycemic targets with diet, exercise, and oral diabetes medications alone (Abstract 467-P).

In the TULIP (Testing the Usefulness of Lantus When Initiated Promptly in Patients With Type 2 Diabetes) study, 66% of patients who began treatment with the long-acting, basal insulin Lantus (insulin glargine [rDNA origin] injection) achieved A1C <7%, the ADA’s recommended target versus 38% of patients assigned to lifestyle management. TULIP was a 9-month, 12-visit, open-label, multinational, multicenter, randomized study.

In an effort to help guide treatment decisions, the ADA and EASD developed a Consensus Algorithm for Type 2 Diabetes that calls for health care providers and diabetes patients to initiate insulin therapy when A1C <7% is not achieved with oral medications and lifestyle management alone, according to a Sanofi-Aventis news release. Physicians typically wait for A1C to approach 9% before adding insulin, however.

“When glycemic targets are not achieved with diet, exercise, and oral medications given at maximum tolerated dose, patients with type 2 diabetes have reached a critical moment in the life cycle of their condition,” said Andre

Grimaldi, MD, Professor Diabetes Department Head, Pitié-Salpêtrière Hospital, Paris. “The results observed in TULIP demonstrate the value of following the ADA/EASD treatment recommendations by initiating basal insulin therapy in a timely manner.”

Phase 3 Alogliptin Results Demonstrated Significant Blood Glucose Reductions

Results of five pivotal phase 3 studies (Abstracts 444-P to 448-P) of the highly selective inhibitor of dipeptidyl peptidase-4 (DPP-4), alogliptin (Takeda Pharmaceutical Company), were announced. The agent is currently under investigation as an oral treatment for type 2 diabetes, according to the company. Alogliptin once daily demonstrated statistically significant reductions in A1C versus placebo as a monotherapy and as an add-on therapy with metformin, thiazolidinediones, insulin, and sulfonylureas.

“Almost half the patients with type 2 diabetes are not at the ADA goal of $\leq 7\%$, so it’s important to have new treatment options that are both effective and well tolerated to potentially address the large number of patients who aren’t adequately controlled,” said Richard Pratley, MD, director of the Diabetes & Metabolism Translational Medicine Unit at the University of Vermont College of Medicine, in a news release. “These clinical data show that alogliptin effectively reduces blood sugar in patients, alone or when used in combination with existing oral antidiabetic treatments as well as insulin, increasing the range of treatment options for patients.”

In all five studies, at 26 weeks, the mean change from baseline A1C levels was significantly greater ($P < .001$) for both 12.5- and 25-mg alogliptin doses versus placebo, respectively:

- alogliptin monotherapy: -0.56%, -0.59%, -0.02%;
- metformin add-on: -0.60%, -0.60%, -0.1%;
- thiazolidinediones add-on: -0.66%, -0.80%, -0.19%;
- insulin add-on: -0.63%, -0.71%, -0.13%; and
- sulfonylurea add-on: -0.38%, -0.52%, +0.01%.

Initial Combination Therapy With Sitagliptin and Metformin Through 2 Years

Initial combination therapy with sitagliptin (Januvia, Merck & Co.), a selective, once-daily DPP-4 inhibitor, and metformin substantially improved markers of beta-cell function and significantly reduced A1C at 1 and 2 years (Abstract 543-P).

According to a news release, sitagliptin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes.

“These 2-year data on initial therapy with sitagliptin and metformin are interesting, particularly to the many physicians who over time need to treat their patients with combination therapy to help achieve and maintain glycemic control,” said Priscilla Hollander, MD, PhD, director, Ruth

Collins Diabetes Center, Baylor University Medical Center.

The US Food and Drug Administration approved sitagliptin in October 2006. It is the first and only DPP-4 inhibitor available in the United States. Initial combination therapy with sitagliptin and metformin significantly improved markers of beta-cell function and significantly improved blood sugar levels compared with either metformin or sitagliptin alone at both 1 year and after 2 years of treatment. The study began with a 24-week, placebo-controlled phase (n=1,091), followed by a 30-week, double-blind, active-controlled period (n=762). The mean baseline A1C of the two populations was 8.8 and 8.7%, respectively. Five-hundred-eighty-seven patients entered into a study extension out to 2 years (including those who had initiated glycemic rescue therapy) and 402 of those patients (mean baseline A1C of 8.6%) were included in the all-patients-treated analysis of efficacy at 2 years.

Saxagliptin Improved Glucose Control in Treatment-Naïve Type 2 Diabetes Patients

Results from a 24-week phase 3 study demonstrated that saxagliptin (Onglyza, Bristol-Myers Squibb and AstraZeneca) produced significant reductions in A1C, fasting plasma glucose, and postprandial glucose in treatment-naïve patients with type 2 diabetes compared with placebo. The adverse event profile appeared similar to placebo (Abstract 517-P).

“Diabetes is a serious and chronic condition that affects nearly 21 million people in the United States and, unfortunately, this number is only going to rise,” said Julio Rosenstock, MD, Director of Dallas Diabetes & Endocrine Center at Medical City, and Clinical Professor of Medicine at University of Texas Southwestern Medical Center, Dallas. “New therapies need to be researched and developed to help treat this growing epidemic,” he said in a news release.

The data represent findings from a multicenter, randomized, double-blind, placebo-controlled, parallel-group study of 401 people with type 2 diabetes (ages 18–77) who were treatment naïve and whose A1C levels were $\geq 7\%$ and $\leq 10\%$. Patients were randomized to one of four treatment arms: saxagliptin 2.5 mg (n=102), 5 mg (n=106), 10 mg, (n=98) or placebo (n=95), once daily.

Rimonabant Significantly Improved Glucose Control in Type 2 Diabetes Patients Treated With Insulin

Rimonabant (Acomplia, Sanofi-Aventis) 20 mg significantly improved A1C by 0.89% from the baseline value, and 0.64% over the control group ($P<.0001$) in ARPEGGIO, the first trial of rimonabant in patients with type 2 diabetes, not adequately controlled with insulin therapy (Abstract 330-OR). Glucose control was three times more pronounced when rimonabant was added than insulin and lifestyle advice alone, according to a news release. The 368 type 2 diabetes patients participating in this 11-month trial had been treated with insulin for an average duration of 6 years

prior to entering the study.

“The ARPEGGIO trial demonstrated that there is still room for significant improvement in diabetic patients who despite several years of standard therapies including insulins, in addition to diet and exercise measures, are not well controlled,” said Priscilla L. Hollander, MD, Baylor University Medical Center, and Coordinating Investigator of the study.

Fewer patients in the rimonabant group compared with controls experienced serious treatment-emergent adverse events (16.8% vs 19.3%, respectively). Anxiety was reported in 5% of the patients in the control arm versus 14% in the rimonabant arm. Depression (including depressed mood) was 7.5% in the control group versus 14% in the rimonabant group; most of the patients had a medical history of depression. Similar numbers of severe hypoglycemia were reported with rimonabant 20 mg/day and control, eight and seven cases, respectively.

NEWS FROM THE ENDOCRINE SOCIETY'S (ENDO) 90TH ANNUAL MEETING

JUNE 15–18, 2008
SAN FRANCISCO

Low Testosterone May Cause Health Problems That Lead to Erectile Dysfunction

Men with erectile dysfunction (ED) should be examined for testosterone deficiency and the metabolic syndrome, as these conditions commonly occur together, a new study presented at ENDO shows (Abstract P3-670)

“[ED] is a portal into men's health,” said the study author, Aksam Yassin, MD, PhD, of the Clinic for Urology and Andrology of the Segeberger Clinics in Norderstedt, Germany. “It is becoming clear that obesity, diabetes, hypertension, hyperlipidemia, and erectile difficulties are intertwined, and a common denominator is testosterone deficiency.”

Dr. Yassin's research sought to determine the prevalence of hypogonadism in men with ED. Over 2 years, investigators looked at 771 patients with an average age of 56 years who were receiving ED treatment. Patients received a comprehensive screening for low testosterone and indicators of the metabolic syndrome. Among the group, 18.3% had testosterone deficiency, which had previously been undetected. The prevalence of hypogonadism in the general population of men aged ≥ 45 years is about 12%, Dr. Yassin said.

Of all the men in the study, 35% had type 1 or type 2 diabetes, and in eight of the men, diabetes was a new diagnosis, according to study data. Hypertension was found in 31%, and 12 of these men had been unaware of it. Among the 21% of men who had dyslipidemia, nine had not previously been diagnosed, and 14% had varying degrees of coronary heart disease. Five of them received this diagnosis for the first time, Dr. Yassin said. Men with ED, especially older men, should therefore receive evaluation not only for ED but also

for testosterone deficiency and any underlying signs of the metabolic syndrome, he advised.

Women Being Recruited to Study Testosterone Gel for Low Libido

Women are being recruited to participate in a new multi-center study of the safety of testosterone gel for postmenopausal women with low sexual desire (Abstract PS-512). The testosterone gel (LibiGel, BioSante Pharmaceuticals) has the “potential to be the first drug approved to treat female sexual dysfunction in menopausal women,” said Michael Snabes, MD, PhD, medical director for BioSante Pharmaceuticals, Inc., in a news release.

“Despite several currently approved pharmaceutical products for men with sexual dysfunction, no drug has been approved in the United States for female sexual dysfunction,” he said. The company seeks to enroll 2,400 to 3,100 women aged 50 to 80 years who have hypoactive sexual desire disorder (HSDD). This condition is the most common type of female sexual dysfunction, affecting 14% to 39% of women. HSDD is the persistent or recurrent absence of sexual fantasies, thoughts and desires, causing the woman distress and results in lower sexual activity. After menopause, a woman’s body produces less testosterone, which may contribute to symptoms of HSDD.

The Endocrine Society has called for more long-term data regarding testosterone use in women.

Women With Diabetes Not Treated as Aggressively as Men

Women with type 2 diabetes and heart disease have poorer control of both diseases and receive less intensive medical treatment than do men, a large new study presented at ENDO found (Abstract P1-327).

The findings of the study, performed at three German universities, may indicate why death due to heart disease has decreased among men with type 2 diabetes but not in women, said lead author Ioanna Gouni-Berthold, MD, Professor of Medicine at the University of Cologne, Germany.

“Our study shows that in patients with diabetes, there is a clear disparity between men and women in the control and treatment of important modifiable risk factors for CVD,” Prof. Gouni-Berthold said. “Women have worse control of their blood pressure, blood sugar and cholesterol levels compared to men and are given cholesterol-lowering medications less often.”

Prof. Gouni-Berthold and colleagues studied nearly 45,000 people with type 2 diabetes treated as outpatients by private practice physicians from 2002 to 2003. Of the patients, 9,521 men and 8,050 women had heart and vascular disease. There were no gender differences in the intensity of medication management or most heart disease risk factors among diabetic patients who did not

have heart disease, the study found.

In the group with CVD, however, women were 44% more likely than men to have high LDL cholesterol, yet 15% less likely to receive lipid-lowering medications, she reported. Women were also 19% more likely than men to have uncontrolled hypertension, women were 15% more likely to have poor long-term control of their blood glucose.

The findings are cause for concern, according to Prof. Gouni-Berthold, because diabetes cancels the protective effect of female gender on the risk of heart disease. “More aggressive treatment of CVD in women with diabetes may improve the gender disparity in CVD mortality,” she said. “Patients should speak with their doctors about the intensity of treatment modalities.”

Moderate Fitness Lowers Mortality Risk in Normal-Weight or Obese Men With Type 2 Diabetes

Being even moderately physically fit lowers male diabetes patients’ risk of death, regardless of their weight (Abstract OR25-2). This study presented at ENDO found that for men with type 2 diabetes, moderate fitness levels reduced the risk of dying of any cause by 40% to 50% during an average follow-up period of 7 years, even if the men were overweight or obese.

“Death rates were the highest for those who were low fit in all weight categories,” said lead investigator Roshney Jacob-Issac, MD, an endocrinology fellow at George Washington University Hospital and the Veterans Affairs (VA) Medical Center in Washington, DC She presented the study results.

Dr. Jacob-Issac and her colleagues studied 2,690 male veterans with diabetes from the Washington, DC, and Palo Alto, Calif, VA hospitals. Of these patients, 406 were a healthy weight, 1,088 were overweight, and 1,196 were obese, as shown by body mass index.

All patients underwent a standard exercise tolerance test. Using a measure of the patients’ peak metabolic rate achieved while exercising, the researchers categorized fitness levels as low, moderate, and high. They found that the higher the level of fitness, the lower the risk of dying during the average 7-year follow-up period. Moderate fitness, compared with low fitness, reduced the death risk by 40% in healthy-weight and overweight men and by 52% in obese individuals. High fitness level further increased this benefit in both healthy-weight and overweight men, to 60% and 65%, respectively. The difference in death risk could not be explained by age, risk factors for heart and vascular disease, or medications, the investigators reported.

Based on the study findings, she recommended, “[Diabetic patients] should improve their fitness level or exercise capacity to at least a moderate level, by being physically active. Weight loss is great, but being active is just as important.” ■