The adage “Moderation in all things” may directly apply to longevity for people with diabetes, according to a national epidemiologic study from Scotland. The study of about 150,000 Scots with type 2 DM found that those with an extremely high – and extremely low – BMI were up to twice as likely to die during the follow-up period as were those with more moderate BMIs.

The study cannot draw any causal links between a moderate BMI and a decrease in mortality, Dr. Jeremy Walker said at the ADA. But it does raise intriguing questions about maintaining a healthy body weight that avoids becoming either over- or underweight. Elevated mortality with higher BMI carries urgent and widely recognized health implications. Elevated BMI is associated with adverse effects on blood pressure, lipid levels, CVD risk, glucose metabolism, and cancer.

While plausible explanations for the relationship between high BMI and death have long existed, explaining the association of low BMI with death is more problematic. Low BMI may actually be a consequence of pre-existing illness rather than a cause. One major study, the Prospective Studies Collaboration (PSC), observed a significant relationship between low-normal BMI and all-cause mortality.

The PSC examined the relationship between all-cause mortality and baseline BMI in almost 1 million subjects included in 57 prospective studies and followed for a mean of 8 years. A very strong U-shaped mortality curve associated with BMI was found. For both genders, the lowest mortality occurred at 22.5-25 kg/m². Each 5 kg/m² higher BMI was associated with about 30% increase in overall mortality. But subjects with lower BMIs were also at an increased risk of death (Lancet 2009;373:1083-96).

Walker et al examined the relationship between mortality and BMI in 150,396 patients with type 2 DM in the Scottish Care Information Diabetes Collaboration. An initial recording of patients’ BMI was linked to national mortality records through 2007, with a mean follow-up of 6 years. The analysis was adjusted for age and socioeconomic status. There were 81,004 males in the cohort, 13,059 of whom had died by 2007. There were 69,392 females, 11,179 of whom had died by the end of the study. The mortality and BMI data showed a strong U-shaped curve, with the lowest mortality in the BMI range of 25 to less than 35. For men with a BMI of 15 kg/m² to less than 20 kg/m², the risk of death was almost double that of men in the 25-35 kg/m² range. The risk of death was 1.5 times increased for men with a BMI of 20 to less than 22.5.

Elevation of risk also was observed for men with a BMI of above 35 to 45 or higher, though the increase was smaller than at the low end of the BMI range. Women faced similar risks. Women with the lowest BMI of 15 to less than 20 kg/m² had almost twice the risk of death as those in the moderate range. Women with the higher BMIs (at least 40) were 1.5 times as likely to die.

Smoking status affected these risks, especially for those with the lowest BMIs. Current male smokers (19,289) with the lowest BMIs were almost 2.5 times more likely to die than those with moderate BMIs. Those with the highest BMIs were 1.75 times as likely to die. Former male smokers (30,962) with the lowest BMIs faced a 1.5 increased risk of death, while those with the highest BMIs were almost 2.5 times more likely to die. Men who never smoked (29,076) had somewhat attenuated mortality risks. Those with the lowest and highest BMIs were around 1.5 times more likely to die than were those in the moderate range. Walker did not present a mortality analysis for women based on smoking status, but confirmed that the U-shaped structure observed for men in each smoking group was also broadly evident for women.
The long-term consequences of diabetes appear to vary even more widely among Asian subgroups than among whites, blacks, and Latinos, according to a new epidemiologic study. The differences in the rates of heart attack, stroke, renal disease, and other problems are so striking among Asians that they warrant a new way of looking at Asians in epidemiology, Alka Kanaya asserted at the annual meeting of the ADA.

“We need to disaggregate the all-Asian data in this country, and around the world, for diabetes surveillance and research,” said Kanaya, an epidemiologist at the University of California, San Francisco. “This is an absolute need. The heterogeneity among these all-Asian groups is greater than the heterogeneity among whites, blacks, and Latinos put together. It actually makes more sense to disaggregate Asians than it does the other ethnic groups.”

Kanaya et al came to this conclusion after examining ethnic differences in diabetes outcomes seen in a large northern California health claims database. From 1996 to 2006, the database collected information on 64,211 subjects with diabetes who reported a single ethnicity. Patients who reported a mixed-race background and those with incomplete racial data were excluded from the analysis.

The study tracked the risks of five diabetes-related outcomes over the 10-year period: myocardial infarction, stroke, heart failure, end-stage renal disease, and lower extremity amputation. Patients were grouped into eight racial/ethnic categories: white (40,286; used as the reference group), black (8,668), Latino (7,763), Filipino (3,572), Chinese (1,823), Japanese (951), Pacific Islander (593), and South Asian (555).

The investigators performed several risk analyses, adjusting for demographics, lifestyle, and disease factors such as diabetes type and duration, HbA1c, hypertension, glomerular filtration rate, albuminuria, and low-density lipoprotein. The study encompassed 415,000 person-years of follow-up data.

In the fully-adjusted model, Pacific Islanders had the highest risk of MI, compared with whites (hazard ratio, 1.53). South Asians had an identical risk to whites; all of the other groups had significantly lower risks. Pacific Island women had the most dramatically elevated risk (HR, 1.93) compared with white women. This was the only significant race/sex association, occurring “in a subgroup that is rarely, if ever, studied individually,” Kanaya said.

The rates for stroke were quite similar to those for heart attack, with significantly decreased risks for Latinos, Filipinos, Chinese, and Japanese. However, Pacific Islanders and South Asians had the same risk as did whites for stroke.

For heart failure, Pacific Islanders, South Asians, and blacks had the same risk as did whites, but all other groups had significantly lower risks.

For lower extremity amputation, all the Asian subgroups except Pacific Islanders had significantly lower risks than did whites: Filipino (HR, 0.39), Japanese (0.51), and Chinese and South Asian (0.44). In Pacific Island subjects, the risk was equal to that seen in the white population.

For end-stage renal disease, “Asians had a huge heterogeneity,” Kanaya said. The risks were significantly elevated in Japanese (2.13), blacks (1.98), Latinos (1.63), Filipinos (1.96), Pacific islanders (1.79), and Chinese (1.50), and were similar to that of whites in South Asians (1.19).

“We can’t be sure of the reasons,” for these differences, Kanaya said. “Some things to look at may be the stress of integration, acculturation, diet, smoking, and attitudes about disease prevention. It’s possible there may also be some kind of unmeasured environmental or biological risk factors.”
Pre- versus postprandial administration of a rapid-acting insulin bolus

The results of a small study suggest that postprandial administration of a mealtime rapid-acting insulin bolus is just as effective as the recommended pre-prandial administration in controlling glycaemia in patients with type 1 diabetes.

Researchers from centres in Beer-Sheva, Israel, studied 12 patients with type 1 diabetes (six using multiple daily injections and six using insulin pumps) in two 3-day periods. In the first period the patients injected the mealtime rapid-acting insulin bolus within the 15 minutes before the meal, as recommended. In the second period the patients injected it immediately after the meal. Patients were monitored by a continuous glucose monitoring system throughout both time periods.

In the postprandial injection period, there was a significantly higher percentage of time during which the patient using an insulin pump, compared to multiple daily injections, were above the recommended upper glucose level of 10 mmol/l (26.5 % versus 8.5 %, respectively). In this same period there were also significantly higher maximal glucose values 2 hours postprandial in patients using an insulin pump (7.8 mmol/l versus 6.7 mmol/l respectively).

The researchers said there were no other significant differences in any of the parameters used to assess glycaemic control between the two time periods. There were also no other significant differences between the patients on multiple injection or pump therapy. Patient satisfaction scores were similar in both time periods. However, more patients preferred postprandial injections, citing the flexibility and a decreased fear of hypoglycaemia.

The researchers concluded that the study found no significant advantage for pre-prandial injection; “It is therefore reasonable to instruct type 1 diabetes patients using multiple daily injections to administer the insulin bolus immediately after the meal, if this timing better suits their lifestyle.” Compliance may also be improved, based on the improved patient satisfaction scores observed in the study.

They noted that patients on pump therapy might need to increase the size of their mealtime bolus if switching from pre- to postprandial administration.

Source: EASD 44th annual scientific meeting, Rome, Italy, 7-11 September 2008, presentation number 1073.

Opinions Differ on Bariatric Surgery for Type 2 DM

Consensus on the role of bariatric surgery for patients with type 2 DM remains elusive, with advocates citing high rates of diabetes resolution and improved survival, and opponents, while acknowledging potential benefits, urging caution until more long-term data are available.

Since 1991, when the U.S. National Institutes of Health’s (NIH) guidelines recommended that bariatric surgery be considered for patients with BMI > 40 kg/m² or > 35 in those with coexisting illnesses such as diabetes, major advances have taken place in surgical experience, techniques, and outcomes. According to U.S. Agency for Healthcare Research and Quality, between 1998 and 2004 there was a 79 % reduction in the mortality rate during hospitalisation following bariatric surgery, Bruce Wolfe said at a congress on interventional therapies for type 2 diabetes.

And 12-month data from the American Society for Metabolic and Bariatric Surgery (ASMBS) now show that after 66,000 procedures, the 30-day mortality rate is 0.3 %, the readmission rate is 5 %, and the rate of re-operations is 2.4 %, said Wolfe, who is professor of surgery at Oregon Health and Science University, Portland.

There have now been eight published studies of various types of bariatric surgery that included some type of comparator group, all showing reductions in mortality ranging from 29 % to 88 %, according to Ted Adams of the University of Utah.

The Conflict

Continued P.4
Surgery is increasingly being done for people with diabetes with BMIs in the 30s. However, conflict exists as to whether to specifically recommend bariatric surgery for them, given that early deaths still occur and uncertainty remains regarding late complications. Some experts believe the evidence is not yet in. "We need to follow these patients for 10-15 years," said Xavier Pi-Sunyer, Professor of Medicine, Columbia University in New York.

A lot of complications are seen in patients who had their surgery 2-3 years ago – bone problems, anaemia, nutritional abnormalities, and hypoglycaemia," Pi-Sunyer said. A safety concern that has increasingly gained attention is the late development of postprandial hypoglycaemia and nesidioblastosis following gastric bypass. While this is not common, it is potentially troublesome. Patients have experienced significant hypoglycaemia resulting in seizures, and approximately 100 patients have had to undergo pancreatectomy, according to Allison Goldfine of Harvard Medical School and Joslin Diabetes Center, both in Boston. Moreover, medical therapy today is successful in many patients, with 55% of patients being able to achieve a HbA1c of 7% or less.

"We need to have more data, obtained by doing a carefully controlled randomised study of sufficient length, perhaps 5 years+, and see if there are subsets of patients who have different risk-benefit ratios," said Hellman, chancellor of the American College of Endocrinology. The surgeons are more enthusiastic. "I don’t have any doubt that patients with BMIs of 40-50 have much to gain from surgery, to which there is a 90% good response," said Mario Morino, professor of general surgery, University of Turin (Italy).

Considerable practical obstacles further complicate the disagreement as to whether indications for surgery should be expanded in type 2 DM to those with lower BMIs. For one thing, costs could exceed $100 million, according to John Buse, of University of North Carolina. In addition, Wolfe noted that when the NIH bariatric surgery consortium was last convened, participants spent a year discussing whether a randomised trial of weight loss surgery should be undertaken, and concluded that such a trial was not feasible, or even necessary.

The Rome Conference

"First we asked the question, reiterating the 1991 [NIH guidelines] statement, ‘Should GIT surgery be considered for patients with type 2 DM and with BMIs >35 who are poorly controlled on medical therapy?’ and there was 100% agreement’ that the answer was yes, Cummings said. “Should we begin use of GIT surgery with lower BMIs (30 and 35) and DM?” 82% agreed. The question was asked whether gastric bypass might be appropriate in this group, and 73% agreed. This may be the most far-reaching item on that a solid consensus was reached. Consensus was not reached on the use of other procedures, such as bilio-pancreatic diversion, duodenal switch, and sleeve gastrectomy.

The Responses

Speaking on behalf of the Obesity Society was Caroline Apovian. “The response so far has been very positive,” she said. “We would like to see more long-term data, but I’m positive we will be able to endorse it”. Representing the AACE, Jeffrey Mechanick said, “We enthusiastically endorse the collaborative efforts to advance the knowledge for surgical intervention through research in type 2 DM. However, we as a society are unable to endorse surgery currently, primarily because of the lack of sufficient long-term data. We need to establish a risk stratification system in type 2 DM and not just rely on a biomarker such as A1c.” Speaking for the ADA was Sue Kirkman, who expressed concerns about the “straw poll” two-thirds majority procedures followed in the Rome conference. The ADA may assemble its own consensus conference, following an iterative process wherein the language of each statement is refined so everyone can agree, she said. We try to be evidence-based, and many times what you think is true doesn’t turn out to be true.”

A different view was expressed by Scott Shikora, chief of bariatrics, Tufts University, Boston. “We wholeheartedly endorse the document,” he said. “We welcome more research – there’s always a benefit to more research – but we feel that we have sufficient to go forward.”