

UROLOGICAL COMPLICATIONS: DEFINITIONS, COST, AND BURDEN

Urinary incontinence (UI) and lower urinary tract symptoms (LUTS) constitute the major symptom-based urinary complications of diabetes¹. Incontinence in women is associated with age, parity, hormonal status and comorbid medical conditions^{2,3}. LUTS, the constellation of irritative and obstructive voiding complaints traditionally associated with benign prostatic hyperplasia (BPH), are nonspecific symptoms attributable to outlet obstruction as well as bladder overactivity, urinary tract infection and other etiologies⁴. Sexual dysfunction is a multidimensional disease concept that encompasses the domains of desire or libido, arousal, and orgasmic function⁵. In men, the dominant domain is arousal (penile erection); in women the interplay of domains is more important and female sexual dysfunction (FSD) is defined by aggregating symptoms from all domains, including pain^{6,7}. Anatomical and physiological differences exist between genders, and contextual and psychological factors may be more important in female sexual dysfunction⁸, as was true in UroEDIC in which depression was the main predictor of FSD in type 1 diabetes.

Female UI, ED, and LUTS/BPH accounted for over 1.2 billion dollars in Medicare annual medical expenditures in 2001. The additional unmeasured costs related to over-the counter-incontinence products, prescription drugs for ED, and complications of severe incontinence such as decubitus ulcers and catheter related infections far exceed the direct costs of treatment. In the United States, urinary incontinence has annual associated costs in excess of \$19 billion⁹. Similarly, the total cost of ED treatments for the 10-20 million affected men in the US exceeds \$3 billion⁵. Although unknown, the per capita cost of treatment for diabetes associated UI and ED is likely to be higher than the cost in non-diabetic patients because of increased severity of symptoms and substantially earlier onset of disease.

DIABETES MELLITUS

Diabetes mellitus is an important cause of morbidity and mortality¹⁰. The Centers for Disease Control and Prevention estimates that diabetes mellitus affected 20 million American adults in 2005. T1D constitutes 5-10% of cases, and incidence is increasing worldwide by 2–5% per year¹¹. The disease burden of T1D is especially significant because of the rising incidence, early age of onset, progressive and irreversible nature of disease, and high rate of complications. Complications of diabetes initiate 18-25% of all inpatient hospital admissions, and represent a major concern for patients, physicians and legislators (Senate Committee on Appropriations Report 107-84). Because the pathogenesis of many diabetic complications is related to hyperglycemia, insights from research in T1D are also relevant to type 2 diabetes (T2D)¹².

Important advances have been made in understanding the pathogenesis of T1D. The disease is due to an autoimmune destruction of pancreatic islet β cells and is associated with cellular and humoral immunological abnormalities¹³. Etiology of T1D is genetically linked with the HLA-DR/DQ locus¹⁴. Patients with T1D become insulin dependent for life; develop late complications; and have a shortened life expectancy. Type 1 diabetes has been linked to long-term complications including retinopathy with potential blindness; nephropathy leading to end stage renal disease; peripheral neuropathy with risk of foot ulcers, amputations, and Charcot joints; and autonomic neuropathy causing cardiovascular, gastrointestinal, and genitourinary symptoms. Patients with T1D also have an increased incidence of atherosclerotic cardiovascular, peripheral arterial, and cerebrovascular disease¹⁵. The morbidity associated with long standing diabetes results from these complications. **Equally as common, although less studied, are the urological complications of diabetes.**

The onset and diagnosis of T1D is occurring earlier in childhood, thus increasing the likelihood of complications and emphasizing the need to identify individuals eligible for interventions such as intensive glycemic control, insulin sensors and pumps, and pharmacoprotective strategies¹⁶. Although most available evidence suggests that the complications of diabetes mellitus are a consequence of metabolic derangements associated with the disease, the substantial variation in onset and severity of complications cannot be fully explained by known risk factors such as duration of diabetes and glycemic control. A genetic basis for microvascular complications such as retinopathy and nephropathy has been suggested from a variety of sources including ethnic, racial and familial differences in risk¹⁷⁻²¹. Future investigations of genetic markers of diabetic complications will need to address issues of population admixture, case numbers, and the characterization of disease phenotypes and covariates. **UroEDIC II can provide the extensive phenotype data for important urological complications of T1D and set the stage for future genetic association studies.**