Urologic Complications of Diabetes: UroEDIC Findings

Aruna V. Sarma, PhD, MHA
University of Michigan
Diabetes Epidemic

Fast Facts on Diabetes

Diabetes

- **Total**: 34.2 million people have diabetes (10.5% of the US population)
- **Diagnosed**: 26.9 million people, including 26.8 million adults
- **Undiagnosed**: 7.3 million people (21.4% are undiagnosed)

- 95% of diabetes cases in the US are associated with Type 2 diabetes (NIDDM)
- 5% associated with Type 1 DM (IDDM) – 85% living as adults
Diabetes and Urological Disorders

Consequences
Diabetes can lead to complications in many parts of the body and increase the risk of dying prematurely.

• Stroke
• Blindness
• Heart attack
• Kidney failure
• Amputation

Urinary Dysfunction
• LUTS
• Incontinence
• UTIs

Sexual Dysfunction
• ED
• FSD
Objectives of UroEDIC

- Assemble a multidisciplinary team: urology, epidemiology, psychiatry, diabetes medicine, neuropathy, genetics
- Determine burden of urological complications of diabetes
- Develop risk factor models for specific urologic complications
- Understand the impact of these conditions on quality of life
- Provide information of importance to health care providers, patients and families about traditionally embarrassing health problems
The Diabetes Control and Complications Trial (DCCT)
- multicenter, randomized clinical trial to compare intensive with conventional diabetes therapy on early vascular and neurologic complications (1983-1993)

Epidemiology of Diabetes Interventions and Complications (EDIC)
- Observational study of the DCCT cohort to examine long term impact of initial randomization and subsequent glycemic control (1994-present)

**DCCT Study Findings**
Intensive blood glucose control reduces risk of
- eye disease 76% reduced risk
- kidney disease 50% reduced risk
- nerve disease 60% reduced risk

**EDIC Study Findings**
Intensive blood glucose control reduces risk of
- any cardiovascular disease event 42% reduced risk
- nonfatal heart attack, stroke, or death from cardiovascular causes 57% reduced risk

Ancillary study to examine burden, onset and risk factors of urologic complications in T1 diabetes
DCCT, EDIC, UroEDIC Timeline

DCCT Baseline
N=761 men
N=680 women

DCCT Closeout
N=746 men
N=676 women

EDIC Baseline
N=741 men
N=675 women

UroEDIC I
N=591 men
N=550 women

UroEDIC II
N=644 men
N=580 women

1983
1993
1994
2003
2010
2016
2021

DCCT 10 Years
EDIC 30 Years

UROEDIC I Baseline (EDIC Year 10)
- Understand the Burden of Urologic Complications in T1DM

UROEDIC II Follow-up (EDIC Years 17-current)
- Incidence, Progression, Risk factors
- Effects of hormonal status and prostate growth
- Quality of Life

EDIC Protocol included UroEDIC
Urological Disorders in UroEDIC

<table>
<thead>
<tr>
<th></th>
<th>Respondents N (%)</th>
<th>Prevalence %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUTS</td>
<td>506 (99)</td>
<td>22</td>
</tr>
<tr>
<td>FSD</td>
<td>297 (58)</td>
<td>42</td>
</tr>
<tr>
<td>UI</td>
<td>493 (97)</td>
<td>31</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUTS</td>
<td>550 (99)</td>
<td>24</td>
</tr>
<tr>
<td>ED</td>
<td>525 (95)</td>
<td>45</td>
</tr>
<tr>
<td>Low desire</td>
<td>506 (92)</td>
<td>40</td>
</tr>
</tbody>
</table>

Figure 1—Study cohort diagram. Flow of participants through the study from DCCT to EDIC and UroEDIC I and II. There were a greater number of participants (1,224) in UroEDIC II compared with UroEDIC I (1,141). *Enrollees were asked to take part in UroEDIC II irrespective of participation in UroEDIC I. There was a net increase in participation from UroEDIC I to UroEDIC II.
Glycemic control and Erectile Dysfunction

- HbA1c at trial baseline associated with 36% increased odds of ED onset 20 years later

- Early glycemic control important for future risk of ED - “Metabolic memory”

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**Table 1. Multivariable logistic regression model of the difference between DCCT intensive vs conventional glycemic therapy in the prevalence of ED**

<table>
<thead>
<tr>
<th>DCCT intervention (intensive vs conventional glycemic therapy)*</th>
<th>OR (95% CI)</th>
<th>p Value (likelihood ratio chi-square test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary prevention cohort</td>
<td>1.24 (0.68, 2.28)</td>
<td>0.49</td>
</tr>
<tr>
<td>Secondary intervention cohort</td>
<td>0.33 (0.18, 0.60)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c at eligibility (per HbA1c%)</td>
<td>1.36 (1.19, 1.56)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes duration (per mo)</td>
<td>1.00 (0.99, 1.01)</td>
<td>0.87</td>
</tr>
<tr>
<td>Age (per yr)</td>
<td>1.13 (1.09, 1.17)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Glycemic control and Urinary Dysfunction

41% increase in odds of UI per HbA1c% increase over the long term - sustained glycemic control

21% increase in UTI count per HbA1c% increase contemporarily - glucotoxic event
Not all about glycemic control

Erectile Dysfunction

![Graph showing incidence rates of ED by antihypertensive medication use.](image)

Table 3. Multivariable Adjusted Hazard Ratios (95% CI)* for Risk of ED by Preceding 3 Year Mean Systolic, Diastolic and Pulse Pressure

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Antihypertensive Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Blood Pressure (per 10mmHg increase)</td>
<td>1.21 (1.04, 1.41)</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (per 10mmHg increase)</td>
<td>1.25 (0.99, 1.59)</td>
</tr>
<tr>
<td>Pulse Pressure (SBP-DBP) (per 10mmHg increase)</td>
<td>1.17 (0.96, 1.42)</td>
</tr>
</tbody>
</table>

*Adjusted for time-dependent versions of Age, Cigarette Smoking and time-weighted HbA1c

Note: Separate Cox proportional hazards models built for each blood pressure variable

Note: Incidence rates of ED are per 1000-person years.
Autonomic neuropathy

Urinary Incontinence in Women

Erectile Dysfunction / LUTS in Men

Figure 2—Prevalence of CAN among women with FSD and UI in DCCT/EDIC. CAN defined as an R-R variation <15 or R-R variation between 15 and 19.9 plus a Valsalva ratio ≤1.5 or a supine-to-standing drop of 10 mmHg in DBP (20).

Figure 3. Prevalence of CAN at DCCT closeout and EDIC year 16/17 by ED and LUTS status at EDIC year 17.
Longitudinal ED and UI Phenotypes

Intermittent Phenotype:
- Traditional Risk Factors (BMI, hysterectomy)
- HbA1c

Persistent Phenotype:
- Autonomic Dysfunction
Urologic Complications and Quality of Life

- Odds of poor QOL defined by lowest quartile of QOL scores
- Effect of ED/UI on poor QOL higher than those observed for other complications
- Participants significantly impacted by urologic disorders
Impact

Medication Adherence

Scope of the Problem

For every 100 prescriptions written...

- 50%-70% are filled at the pharmacy
- 48%-66% are picked up from the pharmacy
- 25%-30% are taken properly
- 15%-20% are refilled as prescribed

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Fringe Benefit of Weight Loss Surgery: Bye, Bye Incontinence?

Written by Kathleen Dobney

Bariatric surgery often produces a welcome fringe benefit for women affected by urinary incontinence (UI). As weight declines, women notice an improvement of the symptoms, or are even cured, according to new research.
Can we do a better job of identifying high risk individuals and can we prevent/treat them?

- Comprehensive study of natural history
- Validate subphenotypes
- Understand mechanisms

Adapted from Agusti et al, Lancet. 2017
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“Urology department. Can you hold?”