

Lower urinary tract symptoms (LUTS) in men with diabetes mellitus

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**All Men
> 40 yrs**

**BPE
Enlargement**

**Diabetic
12-14%**

**BOO
Obstruction 24-35%**

**Histologic
BPH
40-87%**

**LUTS /
Bother
24-90%**

International Continence Society ICS Definitions

Lower urinary tract symptoms (LUTS)- any storage/ voiding symptoms

Storage symptoms- urgency, frequency, urge incontinence, nocturia

Voiding symptoms-hesitancy, slow stream

Benign prostatic hyperplasia (BPH)- Histology

Benign prostatic enlargement (BPE)

Benign prostatic obstruction BPO- UDS prove obstruction in man with BPE

Overactive bladder- Any storage symptoms

Differential Diagnosis

Symptom

Causes

hesitancy, weak stream

- ◆ Obstruction, detrusor overactivity (DO), ↓contractility, Learned

frequency

- ◆ Polyuria, DO, ↓capacity, learned

urgency, urge UI

- ◆ DO, inflammation

nocturia

- ◆ Nocturnal polyuria, DO, ↓capacity

postvoid dribble

- ◆ Postsphincteric collection of urine

BPO versus diabetic cystopathy

◆ BPO

- Urgency, frequency, nocturia
- Slow stream, hesitancy, post void dribble, straining to urinate

◆ Diabetes

- Urgency, frequency early or due to glucosuria
- Straining, hesitancy, infrequent voiding due to cystopathy

Assessment of LUTS

- ◆ American Urologic Association Symptom Score (AUA-SS)
 - Mild 1-7
 - Moderate 8-19
 - Severe 20-35
- ◆ International Prostate Symptom Score (I-PSS)= AUA SS + bother
- ◆ Danish Prostate Symptoms Score (DAN-PSS)

Is there an association between BPH and DM?

Retrospective, n= 432, surgery for BPH, DM were more likely to require intervention¹

12 yr, prospective, n=16,219, highest quartile of glucose correlated with age adjusted risk of requiring BPH surgery, not significant in multivariate Cox regression analysis²

Small non community based samples both association^{1,3} and lack thereof⁴

Population based studies

Boston Aging Study n=2036, 10 yrs, DM not predictive of BPH surge

Beaver Dam Eye Study n=1612, age >48 5 yr longitudinal²

- I-PSS any bother =LUTS, n=100 diabetics
- Overall freq 57%, Nocturia 65%, urge/stream/hesitancy 30%
- Effect of diabetes “borderline”, only CV ds and diuretics

Multinational survey of aging male (MSAM-7) n=14,254, age 50-80³

- 90% have some LUTS on AUAss but 19% sought attention
- DM (13.5%) independent predictor of LUTS

UrEpik n= 4979 men age 40-70, AUA ss⁴

- Moderate to severe LUTS increase from 11% to 40%

Olmsted County 2115 Caucasian men age 40-79, followed 10 yrs
4.6% DM, no difference in prostate size or acute retention⁵

Glynn et al '85; 2. Klein et al'99; 3. Rosen et al '03. 4. Boyle et al'03 5. Burke et al '03 (here)

Retrospective analysis of 9,856 men on tamsulosin for LUTS, 13.1% DM (Type I/II)¹

- Each yr increased odds ratio of diabetes by 4%, I-PSS increased 0.128 pts and residual 0.7 ml
- DM increased IPSS by 1.4 pts and reduced VFR by 1.4 ml/sec
- I-PSS more closely associated with DM than max flow rate or residual urine

Flint Men's Health Study African Amer n=364 age 40-79²

- 30% mod to severe LUTS
- 16.4% diabetics, odds ratio of mod to severe increased in diabetics

If an association between DM and BPH why?

- ◆ Two disorders cause similar symptoms
 - However stronger association than max flow or residual argues against additive effect¹
- ◆ DM influences bladder outlet?
 - Increased α_1 adrenergic tone?
 - Increased prostate growth?
 - Altered detrusor muscarinic sensitivity or afferent?

Diabetic men with BPH and response to therapy

- ◆ Experimental studies suggest enhanced α_1 adrenoceptor function in vascular beds in diabetic animals
- ◆ Tamsulosin study of 9,856 men (13% diabetic)¹
 - Alpha blocker similarly effective in diabetic men
 - Argues against increased α_1 adrenergic tone
 - However observational study, open label

Effect of diabetes on BPH

- ◆ Insulin growth factors (IGF-1 and 3) increased as result of DM and trophic for BPH¹
- ◆ Prostate size larger in in diabetic men²
- ◆ No difference in prostate size over 10 yrs in non DM and DM men in Olmsted County³

Muscarinic receptors

◆ Urethral obstruction

- Increased ?M2
- Muscarinic supersensitivity
- Increased noncholinergic transmission
- Decreased Ach release

◆ Diabetes mellitus¹⁻³

- Enhanced acetylcholine induced contraction by 51%
- Increased number of M receptors
- Increased scopolamine resistance at low freq stim
- **Diuresis causes similar changes!**
- Long term no supersensitivity of carbachol

Effect of BPO on diabetic cystopathy

- ◆ Do residual urine volumes differ in diabetic compared to obstructed men?
 - NO ¹

Common pathophysiology

- ◆ Bladder ischemia
 - De-afferent
 - Detrusor overactivity then fibrosis
 - Cardiovascular ds independent predictor of LUTS
- ◆ Denervation or axopathy
- ◆ Plasticity
 - NGF increased in obstructed bladders (increased afferent sensitivity) and reduced in diabetic bladders (reduced afferent sensitivity)

OM

PO

Bladder

Outlet

Overactive

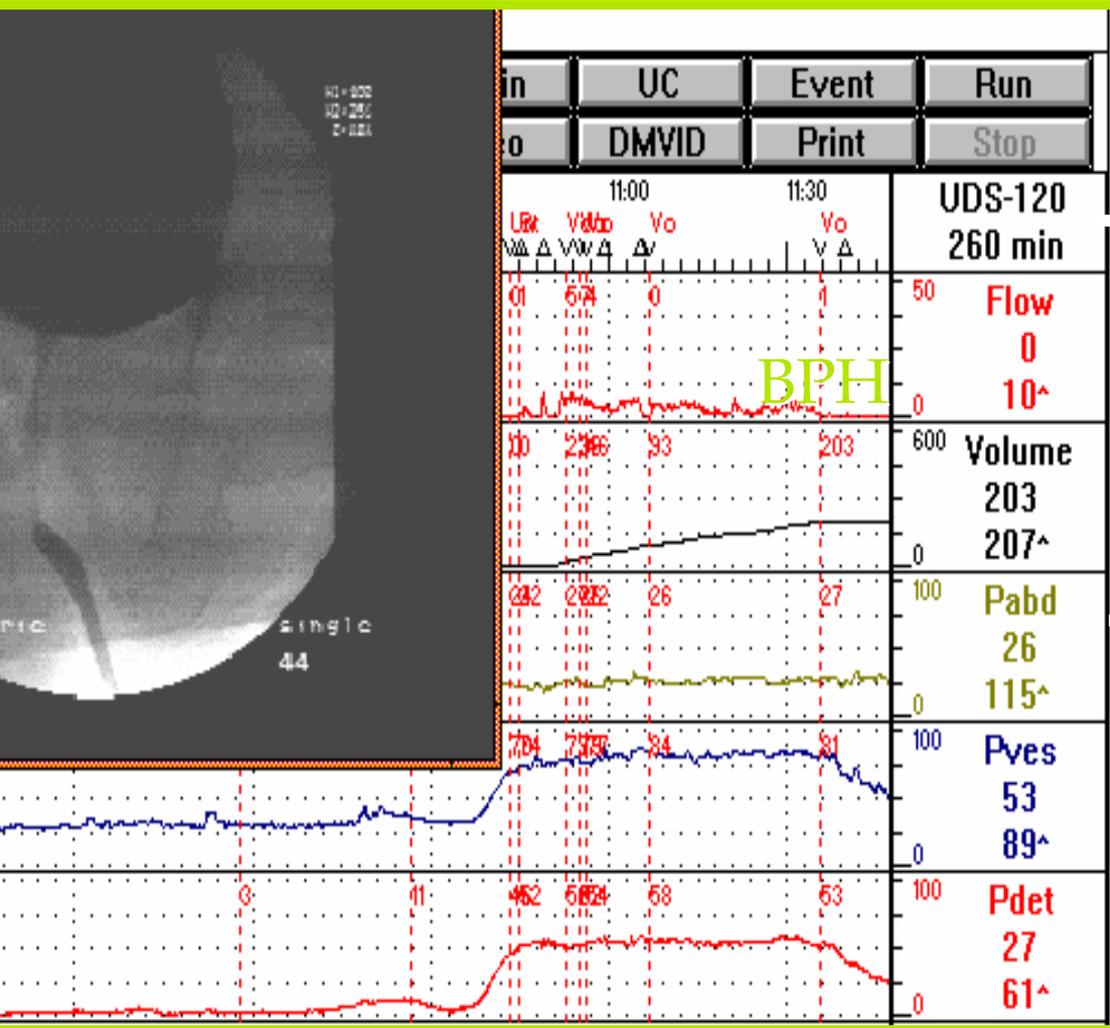
Increased Resistance

Underactive

Reduced Resistance

4 combinations of pathologies resulting in voiding dysfunction!!

BPH (BPO): Normal bladder, increased outlet resistance (functional/anatomic)



	Bladder	Outlet
Overactive		Increased Resistance
Underactive		Reduced Resistance

Urodynamics in diabetic men (DM)

24 DM: 38% cystopathy, 28% obstructed¹

8 diabetic men with decreased stream and PVR²

↓ contractility unrelated to duration or control of DM

↑ residual urine due to ↑ capacity not ↓ contractility since partial cystectomy effective

2 random DM: 28% cystopathy (50% sensation)³

Total AUAss = nonDM but Obstructive score greater in DM

Never saw cystopathy within 5 yrs of onset of DM

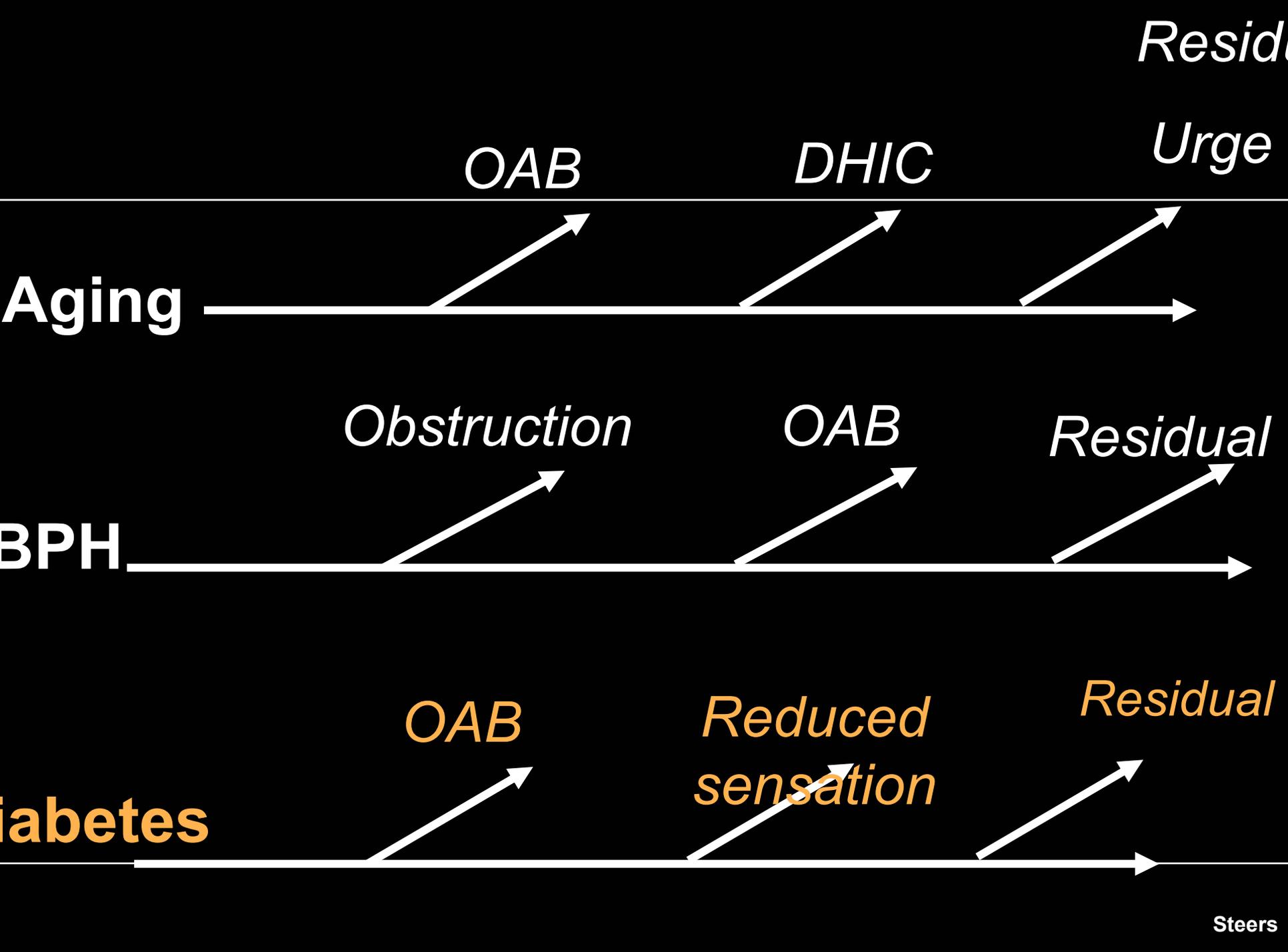
82 DM in urology clinic⁴: 50% overactive, 36% obstructed, 23% hypocontractile, 10% acontractile

2 DM with BPH+LUTS self referred compared to age matched men⁵

No differences in detrusor overactivity (27% vs 46%) or IPSS (15 +/- 9 vs 17 +/- 7)
no difference Type I vs II

End stage diabetes

- ◆ Urodynamics in ESRD vary to diabetes
n=51, Type I, young¹
 - 35% ESRD+DM obstructed
 - 30% decreased sensation
 - 18% hypocontractile
 - 10% detrusor overactivity
- ◆ Diabetic nephropathy not associated with abnormal urodynamics²



What would we like to know

- ◆ Prevalence of diabetic cystopathy
 - Requires large scale , community based, longitudinal studies with urodynamics
- ◆ Prognosis
 - Large numbers of subjects for multivariate analysis- age, co-morbidity BPO adjusted
- ◆ Prevention
 - Identify risk factors-association, temporal relationship, glucose control(HbA1c), cardiovascular disease, etc
- ◆ Sexual dysfunction, UTI, LUTS, BPH and DM mega study because all inter-related