NUOVI APPROCCI ALLE INFEZIONI DELLE VIE URINARIE

Cristina Cornali
U.O. Medicina, Istituto Clinico “S. Anna” – Brescia
Gruppo di Ricerca Geriatrica
Urinary tract infections (UTI) are one of the most common infections in the older population, occurring in the community, hospitals and in long-term care settings.

UTI is incorrectly diagnosed in as many as 40% of hospitalized older people. In European studies, UTI represented 20-26% of nosocomial infections. Between 15 and 25% of UTI have positive blood cultures.

UTI with bacteremia has a high mortality in the older population, with studies reporting a 28 day mortality between 4 and 30%.

UTI are a major source of antimicrobial prescribing in the clinical setting and a potential reservoir for the emergence of resistant organisms.

Community-onset healthcare-related urinary tract infections: Comparison with community and hospital-acquired urinary tract infections

Aguilar-Durana S. et al. (Journal of Infections, 2012)

To analyze the characteristics of infection, adequacy of empirical treatment and outcome of patients with community-onset healthcare-associated (HCA) urinary tract infections (UTI) and compare them with hospital (HA) and community-acquired (CA) UTI.

Results

Epidemiological, clinical and microbiological features suggest that community-onset HCA-UTI is different from CA and similar to HA-UTI.

Patients with community-onset HCA-UTI were older (p = 0.02) had more comorbidities (p = 0.01) and had received previous antimicrobial treatment more frequently than CAUTI (p < 0.01).

Factors related to mortality were

- *P. Aeruginosa* infection  OR 6.51; 95%CI: 1.01–41.73
- Diabetes mellitus  OR 22.66; 95%CI: 3.61–142.21
- Solid neoplasia  OR 22.48; 95%CI: 3.38–149.49
- Age  OR 1.15; 95%CI 1.03–1.28
Healthcare-Bactearemic UTI was defined as an episode detected at hospital admission or within the first 48 h after admission, which fulfilled any of the following:

a) Receiving intravenous therapy, wound care or specialized nursing care at home by qualified healthcare workers within 30 days of the episode

b) Attending a hospital, haemodialysis ward or receiving intravenous chemotherapy within 30 days of the episode

c) Being hospitalized in an acute-care hospital for 2 or more days within 90 days of current hospitalization

d) Residing in a nursing home or long-term care facility

e) Being subjected to an invasive urinary procedure within 30 days of the episode or having a long-term indwelling urethral catheter.
Healthcare-associated, community-acquired and hospital-acquired bacteraemic urinary tract infections in hospitalized patients: a prospective multicentre cohort study in the era of antimicrobial resistance

Horchajada JP, et al. (Clinical Microbiology and Infection, 2012)

Empirical antimicrobials in the groups were:
- 27% cephalosporins
- 22% amoxicillin/clavulanate
- 20% carbapenems
- 14% piperacillin/tazobactam
- 11% fluoroquinolones

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HCA n = 246</th>
<th>CA n = 279</th>
<th>p*</th>
<th>HA n = 142</th>
<th>p**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specific urinary tract symptoms(^a)</td>
<td>94 (38)</td>
<td>183 (66)</td>
<td>&lt;0.001</td>
<td>31 (22)</td>
<td>0.001</td>
</tr>
<tr>
<td>Temperature &gt;38°C</td>
<td>222 (90)</td>
<td>241 (86)</td>
<td>0.17</td>
<td>116 (82)</td>
<td>0.02</td>
</tr>
<tr>
<td>White blood cell count (&lt;4000 or &gt;12000 leucocytes/mm(^3))</td>
<td>167 (68)</td>
<td>174 (63)</td>
<td>0.20</td>
<td>90 (63)</td>
<td>0.59</td>
</tr>
<tr>
<td>Pitt score ≥ 2</td>
<td>98 (40)</td>
<td>86 (31)</td>
<td>0.03</td>
<td>52 (37)</td>
<td>0.53</td>
</tr>
<tr>
<td>Severe sepsis or septic shock</td>
<td>91 (37)</td>
<td>84 (30)</td>
<td>0.09</td>
<td>45 (32)</td>
<td>0.29</td>
</tr>
<tr>
<td>ICU admission</td>
<td>28 (11)</td>
<td>40 (14)</td>
<td>0.31</td>
<td>16 (11)</td>
<td>0.97</td>
</tr>
<tr>
<td>Urological intervention required(^b)</td>
<td>32 (13)</td>
<td>42 (15)</td>
<td>0.50</td>
<td>14 (10)</td>
<td>0.36</td>
</tr>
<tr>
<td>Inappropriate empirical therapy</td>
<td>51 (21)</td>
<td>36 (13)</td>
<td>0.02</td>
<td>40 (28)</td>
<td>0.10</td>
</tr>
<tr>
<td>Median length of stay (range) days</td>
<td>9 (1–66)</td>
<td>7 (0–47)</td>
<td>0.02</td>
<td>13 (0–87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bacteraemia-related in-hospital mortality</td>
<td>12 (5)</td>
<td>5 (2)</td>
<td>0.05</td>
<td>13 (9)</td>
<td>0.10</td>
</tr>
<tr>
<td>All-cause in-hospital mortality</td>
<td>24 (10)</td>
<td>9 (3)</td>
<td>0.002</td>
<td>27 (19)</td>
<td>0.009</td>
</tr>
<tr>
<td>All-cause 30-day mortality</td>
<td>28 (11.4)</td>
<td>11 (3.9)</td>
<td>0.001</td>
<td>29 (20.4)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

HCA, community-onset healthcare-associated; CA, community-acquired; HA, hospital-acquired. Data are given as numbers (%), unless otherwise indicated.

\(^a\)Comparison between HCA and CA.

\(^b\)Comparison between HCA and HA.

\(^a\)Specific urinary tract symptoms included dysuria, frequency, gross haematuria, flank or abdominal pain.

\(^b\)Included endoscopic, percutaneous or surgical drainage, and nephrectomy.
SINTESI

- Pazienti con HCA-UTI vs CA-UTI = maggior comorbidità, maggiori anomalie del tratto genito-urinario, IVU ricorrenti, precedente uso di antibiotici, più rara sintomatologia specifica genito-urinaria.
- Mortalità e degenza ospedaliera più elevate per HCA-UTI vs CA-UTI.
- HCA-UTI e HA-UTI vs CA-UTI = sono causate più frequentemente da batteri resistenti, inclusi produttori di beta-lattamasi, amoxicillin/clavulanic-resistant, and fluoroquinolone-resistant Enterobacteriaceae.
- Pazienti con HCA-UTI dovrebbero essere considerati differenti rispetto a pazienti con CA-UTI, per evitare fallimenti terapeutici, con conseguenti maggior morbidità e mortalità.
- L’isolamento di P. Aeruginosa è significativamente più frequente in pazienti con HA-UTI, ma non in pazienti con HCA-UTI.

(Clinical Microbiology and Infection, 2012)
Signs and symptoms of an infection were reported for 4.0% of the 61,932 eligible residents:

- urinary tract infections 22.3%
- respiratory tract infections 33.6%
- skin and soft tissue infections 21.4%
- conjunctivitis 8%
- gastro-intestinal infections 4.6%

An average annual incidence rate of 4.4 (range: 2.2–6.0) healthcare-associated infections per 1,000 resident-days.

Among the eligible residents, 4.3% received at least one antimicrobial agent:

- amoxicillin-clavulanic acid 12.7%
- nitrofurantoin 10.4%
- trimethoprim 9.9%
- amoxicillin 7.3%
- ciprofloxacin 6.9%

Almost half (48.9%) of all antimicrobial agents were prescribed for a UTI. Uroprophylaxis represented 27.7% of all prescribed antimicrobial agents in participating LTCFs.
BATTERI MULTIRESISTENTI

Prevalence of multidrug-resistant microorganisms increase, both in the hospitals and in long-term care settings

- meticillin-resistant *Staphylococcus aureus* (MRSA)
- extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*
- vancomycin-resistant *Enterococcus* spp. (VRE)

In recent years, Gram-negative bacteria harboring extended beta-lactamase resistance have emerged, particularly but not exclusively *Escherichia coli* and *Klebsiella pneumoniae*. The extended-spectrum beta-lactamases (ESBL) are resistant to many of the antibiotics currently available to treat patients with UTI, including penicillins, cephalosporins and monobactam.

Examples for rates of resistance caused by ESBL:

- hospital = 27.1% for K.Pneumoniae  8.1% for E.Coli
- nursing home = 40.5% for K.Pneumoniae  22% for E.Coli

Epidemiology and resistance patterns in urinary pathogens from long-term care facilities and GP populations.

In 2010, there were 963 urinary isolates from Long-Term Care facilities (LTCF) and 1,169 urinary isolates from General Practitioners (GP), identified from patients 65 years and over, with cytology suggestive of infection.

E. coil was the most common causative organism identified.

Percentages of resistance to antibiotics:

<table>
<thead>
<tr>
<th></th>
<th>LTCF</th>
<th>GP - Community</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>86%</td>
<td>69%</td>
</tr>
<tr>
<td>Amoxicillin-Ac.clavulanic</td>
<td>30%</td>
<td>21%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>58%</td>
<td>26%</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>10%</td>
<td>3%</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>68%</td>
<td>48%</td>
</tr>
<tr>
<td>Piperacillin/tazobactam</td>
<td>10%</td>
<td>4%</td>
</tr>
</tbody>
</table>
Risk Factors for Urinary Tract Infection Caused by Enterobacteriaceae with Extended-Spectrum Beta-Lactamase Resistance in Patients Admitted to Internal Medicine Departments

Vardi M, et al. (IMAJ, 2012)

N. 633 patients.

**Length of hospital stay** = 9.2 ± 12.4 days (median 6 days).

**Total mortality rate** = 32.3% (of these, 22.6% died during hospitalization, 9.7% outside the hospital within 28 days of their admission).

### Parameters correlated to ESBL resistance:
- UTI in the previous 3 months (OR 3.4, \( P < 0.0001 \))
- residency in a long-term care facility (OR 2.4, \( P = 0.004 \))
- presence of a permanent urinary catheter (OR 2.2, \( P = 0.015 \)).

### Predictors of in-hospital mortality:
- dehydration (OR 7.21, \( P < 0.0001 \))
- hypoalbuminemia (OR 5.89, \( P < 0.008 \))
- desaturation at admission (OR 4.43, \( P < 0.0001 \))
- chronic liver disease (OR 11.34, \( P < 0.0001 \))
- concurrent infiltrate in a chest X-ray (OR 8.06, \( P < 0.0001 \)).

### Table:

<table>
<thead>
<tr>
<th>Age (yrs) (average, SD)</th>
<th>81.62 (11.37)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>124 (33.8)</td>
</tr>
<tr>
<td>Female</td>
<td>242 (66.2)</td>
</tr>
<tr>
<td><strong>Mental status</strong></td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td>172 (46.9)</td>
</tr>
<tr>
<td>Normal</td>
<td>138 (37.7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>55 (15.4)</td>
</tr>
<tr>
<td><strong>Functional status</strong></td>
<td></td>
</tr>
<tr>
<td>Debilitated</td>
<td>263 (71.8)</td>
</tr>
<tr>
<td>Normal</td>
<td>91 (24.8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>12 (3.4)</td>
</tr>
<tr>
<td><strong>Residency</strong></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>234 (63.9)</td>
</tr>
<tr>
<td>Long-term care facility</td>
<td>127 (34.6)</td>
</tr>
<tr>
<td>Unknown</td>
<td>5 (1.5)</td>
</tr>
</tbody>
</table>
For community-acquired infections, the most commonly reported risk factors for ESBL-producing *E. coli* infections are *contact with healthcare centers* (recent hospitalization, residence in a long-term care facility, bladder catheterization), recent use of antimicrobial agents, and presence of comorbidities.

Particularly, for UTI acquired in the community, a recent study found that more than 3 UTI episodes in the last year, the use of a beta-lactam antibiotic in the preceding 3 months, and prostate disease were associated with ESBL-producing *E. coli*. 
Causes of *Acute on chronic renal failure* in the elderly

**Toxic injury**
- Bacterial toxins
- Cytokine-induced injury
- Microcirculatory dysfunction
- Apoptosis
- Endothelial injury
- White-cell adhesion

*Fig. 3* Factors causing acute on CRF (*n* = 36)
Studies suggest that UTI is incorrectly diagnosed in as many as 40% of hospitalized older people. The increasing prevalence of healthcare associated infection such as *Clostridium difficile* and emerging antibiotic resistance highlights the importance of obtaining a firm diagnosis, treating with appropriate antibiotics and avoiding the use of broad spectrum antibiotics.

*(Clinical Interventions in Aging, 2011)*
Infezione delle vie urinarie
DEFINIZIONE
(Drugs 2009; Clin Intervention Aging, 2011)

Riscontro di segni clinici e sintomi del tratto genitourinario + la presenza di 1 o più microrganismi nelle urine.

Un’IVU SINTOMATICA necessita della presenza di sintomi come frequenza, urgenza, disuria, nuova incontinenza, tensione in sede costovertebrale o tenesmo vescicale.

L’infezione può essere localizzata a
- vescica (CISTITE)
- parenchima renale (PIELONEFRITE)
- prostata (PROSTATITE BATTERICA ACUTA O CRONICA)

F/M = 50:1

Fattori predisponenti IVU nell’anziano: catetere vescicale, malattie neurologiche che compromettono lo svuotamento vescicale (M. cerebrovascolari, di Alzheimer o di Parkinson), deficit estrogenico post-menopausale, cistocele, incontinenza, malattie prostatiche, calcoli e neoplasie del tratto genitourinario.
<table>
<thead>
<tr>
<th>Term</th>
<th>Standard definition</th>
<th>Application to management of urinary tract infection (UTI) in elderly patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant bacteriuria</td>
<td>Presence of a specified number (usually $&gt;10^5$ CFU/mL) of a single species of bacteria in a freshly voided, midstream specimen of urine.</td>
<td>This level of bacteriuria is significant because it is unlikely that it can be explained by contamination of the urine sample with perineal flora. It DOES NOT indicate clinically significant bacteriuria. “Significant” bacteriuria is often asymptomatic and does not necessarily require treatment. Lower levels may sometimes be significant. The evidence about effectiveness of short (3 day) courses of treatment for UTI only applies to uncomplicated UTIs. All UTIs in males, all UTIs associated with urinary catheters, and all UTIs with systemic symptoms are complicated UTIs. Both nitrofurantoin and fosfomycin only achieve effective concentrations in the lower urinary tract infection. These antibiotics should not be used to treat patients with systemic symptoms or signs.</td>
</tr>
<tr>
<td>Uncomplicated urinary tract infection</td>
<td>Lower urinary tract infection in an adult woman who is not pregnant and has no underlying abnormality of the urinary tract or indwelling urinary device.</td>
<td></td>
</tr>
<tr>
<td>Lower urinary tract infection</td>
<td>Infection confined to the tissues of the bladder or urethra. The presence of symptoms or signs of systemic infection indicates upper urinary tract infection.</td>
<td></td>
</tr>
</tbody>
</table>
Clinical presentation of urinary tract infection (UTI) differs with aging in women

Arinzon Z, et al. (Arch Gerontol Geriatr 2012)

196 women aged a minimum of 45 years with diagnosis of UTI (= uropathogen > $10^3$ cfu/ml in urine culture)

The patients were divided into two groups:

- Pre-menopausal ($n = 102$, mean age 48.1 years)
  → local symptoms: frequency, painful and burning of urination, bladder pain

- Post-menopausal ($n = 94$, mean age 69.2 years)
  → predominantly generalized unspecific symptoms + storage symptoms, urgency of urination, painful voiding, urinary incontinence, sexual activity, low-back pain, lower abdominal pain
Infezione delle vie urinarie
DIAGNOSI DI IVU NELL’ANZIANO

(Drugs 2009; Clin Intervention Aging, 2011)

- Many clinicians incorrectly attribute factors such as functional decline, increased confusion, and nonspecific signs and symptoms to UTI and start treatment on this basis.
- Nonspecific signs, such as change in function, malaise, and falls are not significantly associated with bacteriuria plus pyuria.

Antibiotics should be initiated for old disabled patients without a urinary catheter with acute dysuria alone or fever (defined as temperature above 38°C) and 1 of genitourinary symptoms:
- new or worsening urgency and frequency
- suprapubic pain
- frank hematuria
- costovertebral angle tenderness
- urinary incontinence.

Altered mental status may not be per se a useful criterion for commencing antibiotics, but dysuria, change in character of urine and change in mental status were significantly associated with bacteriuria plus pyuria in patients with suspected UTI.
- Absence of these clinical features identified patients at low risk (25.5%)
- Presence of dysuria plus one or both of the other clinical features identified patients at high risk (63.2%).
Challenges in Assessing Nursing Home Residents with Advanced Dementia for Suspected Urinary Tract Infections


Although mental status and rigor were not included in the original guidelines for noncatheterized NH residents, it was decided to include them given the inability of residents with advanced dementia to express other symptoms.

Table 1. Minimum Criteria for Initiation of Antimicrobial Therapy Use for Suspected Urinary Tract Infection in Nursing Home (NH) Residents with Advanced Dementia

<table>
<thead>
<tr>
<th>No indwelling Foley catheter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute dysuria or fever (single oral temperature &gt;100°F (&gt;37.8°C), oral temperature &gt;99°F (&gt;37.2°C) ≥ 2 times, or increase in temperature &gt;2°F (&gt;1.1°C) over baseline temperature) and ≥ 1 of</td>
</tr>
<tr>
<td>New or worse urinary frequency</td>
</tr>
<tr>
<td>Urgency</td>
</tr>
<tr>
<td>Costovertebral tenderness</td>
</tr>
<tr>
<td>Gross hematuria</td>
</tr>
<tr>
<td>Suprapubic pain</td>
</tr>
<tr>
<td>Mental status change</td>
</tr>
<tr>
<td>Rigor</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Indwelling Foley catheter ≥ 1 of</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (single oral temperature &gt;100°F (&gt;37.8°C), oral temperature &gt;99°F (&gt;37.2°C) ≥ 2 times, or increase in temperature &gt;2°F (&gt;1.1°C) over baseline temperature)</td>
</tr>
<tr>
<td>Rigor</td>
</tr>
<tr>
<td>Change in mental status</td>
</tr>
</tbody>
</table>

Loeb M, Bentley DW, Bradley S et al. Infect Control Hosp Epidemiol 2001
Challenges in Assessing Nursing Home Residents with Advanced Dementia for Suspected Urinary Tract Infections


N.266, age 86.6±7.4 years, 85.7% female, 4.1% with a urinary catheter. Mean follow-up time = 221.2±131.8 days.

N.72 (27.1%) of 266 residents experienced 131 suspected UTIs (a mean of 2 suspected UTI episodes/person).

In 79.2% of suspected UTI episodes, both urinalyses and cultures were positive. This percentage was not statistically significantly different between episodes that met and did not meet minimum symptoms or signs to initiate antimicrobial therapy.

74.5% of episodes that did not meet minimum criteria were treated with antimicrobial therapy. Mental status change was more commonly documented in noncatheterized than catheterized residents (48.3% vs 13.3%) and fever was less commonly documented in noncatheterized than catheterized residents (19.0% vs 33.3%). The proportion of episodes for which the minimum criteria to initiate antimicrobial therapy were met based on symptoms and signs was lower in noncatheterized residents (12.9% vs 40.0%).

This study demonstrates that UTIs are commonly suspected in NH residents with advanced dementia but that the great majority of these episodes probably do not reflect a true UTI, resulting in substantial inappropriate antimicrobial exposure.
Dipstick testing need to provide evidence:

- with a positive test, the probability of bacteriuria was 51 - 73%
- with a negative test, the probability of bacteriuria was 9 - 21%
- the combination of negative leukocyte and nitrite test had a NPV of 88% (95%CI: 84–92%)

These results are similar to the positive and negative predictive value of clinical symptoms and signs without stick testing.

Pyuria represents the presence of white blood cells in urine and suggests an underlying inflammation of the genitourinary tract. WBC may be present without bacteriuria and are particularly associated with the presence of a urinary catheter, stone, tumor, or infection of the lower genital tract.

(Drugs 2009; Clin Intervention Aging, 2011; Curr Opin Infect Dis, 2012)
Urine cultures should not be sent in individuals who are asymptomatic.

- Urine culture does not establish the diagnosis of UTI, but in the elderly it is important obtaining cultures prior to commencing antibiotics.
- Repeat urine cultures following treatment as a “test of cure” are not recommended because of the high prevalence of asymptomatic bacteriuria in the elderly.
- Urine specimens for culture should be processed as soon as possible, preferably within 1–2 h.
- If urine specimens cannot be processed within 30 min of collection, they should be refrigerated. Refrigerated specimens should be cultured within 24 h.

(Drugs 2009; Clin Intervention Aging, 2011; Curr Opin Infect Dis, 2012; Infect Control Hosp Epidemiol, 2012)
Asymptomatic bacteriuria

*Clinical Interventions in Aging, 2011*

- Studies have suggested a prevalence rate of 25 – 50% of women and 15 – 40% of men without catheters among nursing home residents.
- It requires confirmation by two consecutive samples.
- It should not be treated with antibiotics in the elderly population.
- Treating asymptomatic bacteriuria does not reduce mortality and can cause harm.
INFEZIONI DELLE VIE URINARIE ASSOCIATE A CATETERE VESCICALE
Catheter-associated UTI

- Indwelling urinary catheters lead to almost universal bacteriuria within 3–4 days of catheterization.
- The vast majority of asymptomatic catheter-associated bacteriurias do not progress to symptomatic infection.
- The majority of cases of nosocomial CAUTI are asymptomatic bacteriuria, that is not a clinically significant condition, and treatment is unlikely to confer clinical benefit. Its inappropriate treatment is potentially harmful in terms of emergence of resistant pathogens, suprainfections, and unnecessary costs.
- Collecting more urinalyses and urine cultures at admission, even on asymptomatic patients, leads to increased inappropriate use of antibiotics.
- Catheter samples of urine should only be sent if the patient shows signs of sepsis.
- If CAUTI is probable, urinary catheters should ideally be removed and a culture acquired from a freshly inserted catheter prior to commencing antimicrobials.

(National Institute of Health, 2010; Clinical Interventions in Aging, 2011; Curr Opin Infect Dis, 2012)
Catheter-associated UTI

Criteria for symptomatic CAUTI

- symptoms **plus** a positive urine culture of $\geq 10^5$ CFU/ml
  
  OR

- symptoms **plus** a positive urine culture of between $10^3$ and $10^5$ CFU/ml **AND**
  the presence of a positive urinalysis (as defined by a positive dipstick with pyuria or microorganisms)

  *(Center of Disease Control, 2009)*

- In patients with indwelling urinary catheters who are pyrexial, the clinician should exclude other sources of infection and look for any localizing signs such as suprapubic tenderness or loin pain

  *(Scottish Intercollegiate Guidelines Network 2006)*

- New or worsening fever, rigors, altered mental state, general malaise, or lethargy without other identified causes were identified as possible signs and symptoms

  *(Infectious Diseases Society of America, 2009)*
Surveillance Definitions of Infections in Long-Term Care Facilities: Revisiting the McGeer Criteria

Nimalie D. Stone, MD; Muhammad S. Ashraf, MD; Jennifer Calder, PhD; Christopher J. Crnich, MD; Kent Crossley, MD; Paul J. Drinka, MD; Carolyn V. Gould, MD; Manisha Juthani-Mehta, MD; Ebbing Lautenbach, MD; Mark Loeb, MD; Taranisia MacCannell, PhD; Preeti N. Malani, MD; Lona Mody, MD; Joseph M. Mylotte, MD; Lindsay E. Nicolle, MD; Mary-Claire Roghmann, MD; Steven J. Schweon, MSN; Andrew E. Simor, MD; Philip W. Smith, MD; Kurt B. Stevenson, MD; Suzanne F. Bradley, MD

for the Society for Healthcare Epidemiology Long-Term Care Special Interest Group*

*Presented at the AHA 2012, November 16, San Antonio, TX.
Definitions of Urinary Tract Infections in Long-Term Care Facilities

PERSONE SENZA CATETERERE VESCICALE

1. At least 1 of the following sign or symptom subcriteria
   a. Acute dysuria or acute pain, swelling, or tenderness of the testes, epididymis, or prostate
   b. Fever or leukocytosis (see Table 2) and at least 1 of the following localizing urinary tract subcriteria
      i. Acute costovertbral angle pain or tenderness
      ii. Suprapubic pain
      iii. Gross hematuria
      iv. New or marked increase in incontinence
      v. New or marked increase in urgency
      vi. New or marked increase in frequency
   c. In the absence of fever or leukocytosis, then 2 or more of the following localizing urinary tract subcriteria
      i. Suprapubic pain
      ii. Gross hematuria
      iii. New or marked increase in incontinence
      iv. New or marked increase in urgency
      v. New or marked increase in frequency

2. One of the following microbiologic subcriteria
   a. At least $10^5$ cfu/mL of no more than 2 species of microorganisms in a voided urine sample
   b. At least $10^2$ cfu/mL of any number of organisms in a specimen collected by in-and-out catheter
Definitions of Urinary Tract Infections in Long-Term Care Facilities

PERSONE CON CATETERE VESCICALE A PERMANENZA

1. At least 1 of the following sign or symptom subcriteria
   a. Fever, rigors, or new-onset hypotension, with no alternate site of infection
   b. Either acute change in mental status or acute functional decline, with no alternate diagnosis and leukocytosis
   c. New-onset suprapubic pain or costovertebral angle pain or tenderness
   d. Purulent discharge from around the catheter or acute pain, swelling, or tenderness of the testes, epididymis, or prostate
2. Urinary catheter specimen culture with at least $10^5$ cfu/mL of any organism(s)

Criterio di nuova inclusione.
Alterazioni dello stato cognitivo-funzionale possono essere causate da altri fattori, ma la necessità della presenza di LEUCOCITOSI e l’ESCLUSIONE di diagnosi alternative, supporta l’eziologia infettiva.

In ogni caso, l’IVU sintomatica in persone catetereizzate, in assenza di sintomi genitourinari, deve sempre essere una diagnosi di esclusione.

Se catetere è stato posizionato da più di 14gg, l’urocultura va raccolta dopo sostituzione del catetere

Criterio presente sia per persone senza sia con catetere vescicale
Appropriate Indications for Indwelling Urethral Catheter Use

- Patient has acute urinary retention or bladder outlet obstruction
- Neurogenic bladder dysfunction and urinary retention
- Need for accurate measurements of urinary output in critically ill patients
- Perioperative use for selected surgical procedures:
  - Patients undergoing urologic surgery or other surgery on contiguous structures of the genitourinary tract
  - Anticipated prolonged duration of surgery (catheters inserted for this reason should be removed in PACU)
  - Patients anticipated to receive large-volume infusions or diuretics during surgery
  - Need for intraoperative monitoring of urinary output
- To assist in healing of open sacral or perineal wounds (stage III or IV) in incontinent patients
- Patient requires prolonged immobilization (e.g., potentially unstable thoracic or lumbar spine, multiple traumatic injuries such as pelvic fractures)
- To improve comfort for End-of-Life care if needed
Inappropriate Uses of Indwelling Catheters

- As a substitute for nursing care of the patient or resident with incontinence
- As a means of obtaining urine for culture or other diagnostic tests when the patient can voluntarily void
- For prolonged postoperative duration without appropriate indications (e.g., structural repair of urethra or contiguous structures, prolonged effect of epidural anaesthesia, etc.)
Minimize urinary catheter use and duration of use in all patients, particularly those at higher risk for CAUTI or mortality from catheterization such as women, the elderly, and patients with impaired immunity (Evidence IB).

Avoid use of urinary catheters in patients and nursing home residents for management of incontinence (Evidence IB).

Further research is needed on periodic (e.g., nighttime) use of external catheters (condom catheters) in incontinent patients or residents and the use of catheters to prevent skin breakdown (No recommendation/unresolved issue).

Use urinary catheters in operative patients only as necessary, rather than routinely (Evidence IB).

For operative patients who have an indication for an indwelling catheter, remove the catheter as soon as possible postoperatively, preferably within 24 hours, unless there are appropriate indications for continued use (Evidence IB).
Reducing Inappropriate Urinary Catheter Use

(Arch Intern Med, Feb 2012)

Despite the apparent simplicity of these guidelines, programs seeking to reduce CAUTI have to overcome well-defined barriers involving health care providers, including

1) lack of knowledge of the criteria for appropriate urinary catheter use
2) failure to recognize that a urinary catheter is present, particularly if the catheter was placed elsewhere
3) failure to remove the catheter at the appropriate time.
How to reduce Urinary Catheter Use

- Face-to-face reminders involving nurses and clinicians on removal of catheter, usually 4 days after catheterization, or to insert it only when absolutely necessary

- Alternatives to indwelling urethral catheterization in patients who require measurement of urinary output or relief from obstruction:
  - condom catheters
  - suprapubic catheterization (more comfortable and acceptable; lower incidence of CAUTI)
  - intermittent catheterization
Pickard R, et al.

Antimicrobial catheters for reduction of symptomatic urinary tract infection in adults requiring short-term catheterisation in hospital: a multicentre randomised controlled trial.

(Lancet, December 2012)

N.6394 subjects (99% surgical patients).
After short-term catheterisation (<14 days, median 2 days), incidence of CAUTI was measured with

a) silver-alloy urinary catheters (N.2097 – incidence 12.5%)
b) nitrofural-impregnated urinary catheters (N.2153 – incidence 10.6%)
c) standard polytetrafluoroethylene urinary catheters (N.2144 – incidence 12.6%)

No clinically relevant difference was noted between the 3 groups.
Prevention of CAUTI: *simple is beautiful*

Marc Leone, Service d’Anesthésie et de Réanimation, Assistance - Publique–Hôpitaux de Marseille, Aix Marseille Université  
*(Lancet, December 2012)*

**Comment**

- In countries where health-care costs are sustained by the community, such funding is crucial to provide clear and objective responses to pragmatic issues, independent of commercial pressures.
- For urinary drainage systems, in terms of prevention of CAUTI, simplicity should be the rule. Expensive devices are not synonymous with improved health care.
- Even if the rate of positive bacteriuria was significantly reduced in the participants receiving the nitrofural-impregnated catheter, they reported more discomfort.
- Standard latex catheters, which are safe and comfortable, should be recommended for routine short-term use.
- Future guidelines might reserve a place for the nitrofural-impregnated catheter in specific populations of patients, such as those at high risk of severe sepsis, immunosuppressed, or undergoing urological procedures.
INFEZIONI DELLE VIE URINARIE

PREVENZIONE
**Infezione delle vie urinarie**

**DEFINIZIONE IVU RICORRENTI**

*(Drugs 2009; Clin Intervention Aging, 2011)*

**IVU ricorrenti** si verificano in più di 1/3 delle donne dopo un primo episodio. Il trattamento delle forme ricorrenti è necessario dopo 2+ episodi in 6 mesi o 3+ episodi in 1 anno (*NB* = definizione valida solo per *giovani donne* con IVU non complicate).

Per la **prevenzione** delle IVU ricorrenti, grande interesse è stato rivolto agli approcci non-antibiotici: uso di probiotici, vaccini, oligosaccaridi inibitori dell’adesione e colonizzazione batterica della mucosa genitourinaria, estratti immunoreattivi di E.Coli che interferiscono con il ciclo vitale batterico. Il trattamento preventivo con estrogeni intravaginali ha ottenuto risultati contrastanti.
Prevention of urinary tract infections in nursing homes: lack of evidence-based prescription?

Bergman J, Schjøtt J, Blix HS. (BioMedCentral Geriatrics, 2011)

1473 residents in 44 Norwegian nursing homes

18% had at least 1 agent recorded as prophylaxis of UTI

1) 48% Methenamine - Esametilentetretamina (Antisettico urinario prodotto della condensazione dell'ammoniaca e della formaldeide. Deve le sue proprietà antibatteriche al fatto che si decompone liberando formaldeide. Gran parte dei batteri sono sensibili alla formaldeide libera senza sviluppare resistenza; è particolarmente attiva verso E.Coli e dei Gram- negativi, a eccezione di Enterobacter aerogenes e Proteus vulgaris. Somministrata per os come ippurato o mandelato. Controidicata nei pazienti con insufficienza epatica)

2) 32% Vitamin C

3) 30% Estrogens, but only 1/3 for vaginal administration

4) 10% Cranberry products

5) 5% Trimethoprim

6) 4% Nitrofurantoin

Conclusions: prescribing of prophylactic agents for UTIs in nursing homes is not evidence-based according to the literature and current national guidelines.
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Vaginal estrogens have been shown to decrease UTI while systemic estrogens do not appear to have the same effect. Systemic estrogens have been associated with increased risk of cardiovascular disease, venous thromboembolic events and breast cancer. Some guidelines recommend vaginal estrogens to women with recurrent UTI.
Prevention of urinary tract infections in nursing homes: lack of evidence-based prescription?

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Cranberry products in a variety of formulations have also undergone extensive evaluation over several decades. Cranberry appears to work by inhibiting the adhesion of type I and P-fimbriated uropathogens (e.g. uropathogenic E. coli) to the uroepithelium. The isolation of the components of cranberry with this activity (anthocyanidin moieties) has been a daunting task, considering the hundreds of compounds found in the fruit and its juice derivatives. Problems still exist with standardization of cranberry products and evaluation of specific key cranberry-derived compounds considered likely to be active moieties.

In general, the preventive efficacy of cranberry has been variable and modest. Meta-analyses have established that recurrence rates over 1 year are reduced approximately 35% in young to middle-aged women.

The efficacy of cranberry in other groups (i.e. elderly, paediatric patients, those with neurogenic bladder, those with chronic indwelling urinary catheters) is questionable.

Adverse events include gastrointestinal intolerance, weight gain (due to the excessive calorie load) and drug-cranberry interactions (due to the inhibitory effect of flavonoids on cytochrome P450).

The findings of the Cochrane Collaboration support the potential use of cranberry products in the prophylaxis of recurrent UTIs in young and middle-aged women. However, in light of the heterogeneity of clinical study designs and the lack of consensus regarding the dosage regimen and formulation to use, cranberry products cannot be recommended for the prophylaxis of recurrent UTIs at this time.
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Conclusions: prescribing of prophylactic agents for UTIs in nursing homes is not evidence-based according to the literature and current national guidelines.
UROPATIA OSTRUTTIVA & VESCICA NEUROLOGICA
come fattori predisponenti le Infezioni urinarie
78% dei pazienti sottoposti a intervento di artroprotesi d’anca possono sviluppare una ritenzione acuta d’urina

<table>
<thead>
<tr>
<th>Table 1. Selected Causes of Urinary Retention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cause</strong></td>
</tr>
<tr>
<td>Obstructive</td>
</tr>
<tr>
<td>Infectious and inflammatory</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

**Note:** The text in blue represents the Italian translation of the table.
<table>
<thead>
<tr>
<th>Class</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiarrhythmics</td>
<td>Disopyramide (Norpace); procainamide (Pronestyl); quinidine</td>
</tr>
<tr>
<td>Anticholinergics (selected)</td>
<td>Atropine (Atreza); belladonna alkaloids; dicyclomine (Bentyl); flavoxate (Urispas); glycopyrrolate (Robinul); hyoscymamine (Levsin); oxybutynin ( Ditropan); propantheline (Pro-Banthine*); scopolamine (Transderm Scop)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Amitriptyline (Elavil*); amoxapine; doxepin (Sinequan*); imipramine (Tofranil); maprotiline (Ludiomil*); nortriptyline (Pamelor)</td>
</tr>
<tr>
<td>Antihistamines (selected)</td>
<td>Brompheniramine (Brovex); chlorpheniramine (Chlor-Trimeton); cyproheptadine (Periactin*); diphenhydramine (Benadryl); hydroxyzine (Atarax*)</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>Hydralazine; nifedipine (Procardia)</td>
</tr>
<tr>
<td>Antiparkinsonian agents</td>
<td>Amantadine (Symmetrel); benztrapine (Cognent); bromocriptine (Parlodel); levodopa (Larodopa*)†; trihexyphenidyl (Artane*)</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Chlorpromazine (Thorazine*); fluphenazine (Prolixin*); haloperidol (Haldol); prochlorperazine (Compazine*); thioridazine (Mellaril*); thiothixene (Navane)</td>
</tr>
<tr>
<td>Hormonal agents</td>
<td>Estrogen; progesterone; testosterone</td>
</tr>
<tr>
<td>Muscle relaxants</td>
<td>Baclofen (Lioresal); cyclobenzaprine (Flexeril); diazepam (Valium)</td>
</tr>
<tr>
<td>Sympathomimetics (alpha-adrenergic agents)</td>
<td>Ephedrine; phenylephrine (Neo-Synephrine); phenylpropanolamine‡; pseudoephedrine (Sudafed)</td>
</tr>
<tr>
<td>Sympathomimetics (beta-adrenergic agents)</td>
<td>Isoproterenol (Isuprel); metaproterenol (Alupent); terbutaline (Brethine*)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Amphetamines; carbachazepine (Tegretol); dopamine (Intropin*); mercurial diuretics; nonsteroidal anti-inflammatory drugs (e.g., indomethacin [Indocin]); opioid analgesics (e.g., morphine [Duramorph]); vincristine (Vincasar PFS)</td>
</tr>
</tbody>
</table>
Circa il 55% dei pazienti con stroke possono avere ritenzione acuta d'urina, principalmente per iporeflexia detrusoriale. La maggior parte ha una risoluzione a 3 mesi.

Oltre 45% dei pazienti con DM e il 75-100% con neuropatia periferica diabetica possono sviluppare ritenzione acuta d'urina.

Table 3. Neurologic Causes of Urinary Retention and Voiding Dysfunction

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autonomic or peripheral nerve</td>
<td>Autonomic neuropathy; diabetes mellitus; Guillain-Barré syndrome; herpes zoster virus; Lyme disease; pernicious anemia; poliomyelitis; radical pelvic surgery; sacral agenesis; spinal cord trauma; tabes dorsalis</td>
</tr>
<tr>
<td>Brain</td>
<td>Cerebrovascular disease; concussion; multiple sclerosis; neoplasm; tumor; normal pressure hydrocephalus; Parkinson’s disease; Shy-Drager syndrome</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>Myelomeningocele; myelocele; hematoma or abscess; spinal cord trauma; spinal stenosis; spinovascular disease; transverse myelitis; tumors or masses of conus medullaris or cauda equine</td>
</tr>
</tbody>
</table>
Uropatie ostruttive
TRATTAMENTO INIZIALE

- Acute urinary retention should be managed by immediate and complete decompression of the bladder through **catheterization**.
- Hematuria, hypotension, and postobstructive diuresis are potential complications of rapid decompression. However, there is no evidence that gradual bladder decompression will decrease these complications.
- In patients with known or suspected BPH, the optimal amount of time to leave a catheter in place is unknown.
- If the bladder is simply drained, > 70% of men will have another episode of urinary retention within 1 week.
- Men with BPH have a greater chance of a successful voiding trial without a catheter if they are treated with alpha-adrenergic blockers for 3 days starting at the time of catheter insertion.

*(Selius BA, American Family Physician, 2008)*
Rehabilitation in practice: neurogenic lower urinary tract dysfunction and its management.

Panicker JN, de Sèze M, Fowler CJ. (Clinical Rehabilitation, 2010)

Clinical messages

- History, bladder diary, measurement of post void residual urine form the cornerstone of the evaluation of neurogenic lower urinary tract dysfunction. Urodynamics are useful in evaluating and following up lower urinary tract dysfunction in several situations.
- Antimuscarinic medications are the first line treatment for detrusor overactivity and newer agents may be associated with less side-effects.
- Clean intermittent self catheterization is the preferred management for impaired voiding.
- Injection of botulinum toxin A into the detrusor muscle appears to be a promising treatment for refractory detrusor overactivity.

Ultrasonography is used to assess the degree of incomplete bladder emptying, and for assessing the upper tracts. Urodynamic tests assess detrusor and bladder outlet function and give fundamental information about detrusor pressure and thus the risk factor for upper tract damage.

Self-catheterization should be initiated if the post-void residual urine is > 100 mL or exceeds 1/3 of bladder capacity.
Intermittent self catheterisation with hydrophilic, gel reservoir, and non-coated catheters: a systematic review and cost effectiveness analysis
Bermingham SA, et al. (BMJ, 2013)

Objective
To determine the most effective and cost effective type of catheter for patients performing intermittent self catheterisation in the community.

Main outcome measures
Clinical outcomes included symptomatic urinary tract infection (UTI), bacteraemia, mortality, patient preference or comfort, and number of catheters used.
The economic model included downstream complications of UTI and cost effectiveness was calculated as incremental cost per quality adjusted life years (QALYs) gained.
Conclusions

- Given current understanding of the scope of antibiotic resistance, multiple use non-coated catheters are the most cost effective option for intermittent self catheterisation.
- There was no significant difference in the incidence of symptomatic UTI for people using clean versus sterile non-coated catheters for long term intermittent self-catheterisation.
- Compared with clean non-coated catheters changed once weekly, clean non-coated catheters changed once daily and sterile non-coated catheters changed once per use are less effective and more expensive; they are therefore not cost effective.
- Hydrophilic catheters are less effective than gel reservoir and their cost per QALY gained compared with clean non-coated catheters (changed once weekly) is higher.
- Compared with hydrophilic catheters, gel reservoir catheters are cost effective.
- If clean non-coated catheters are not considered a viable option for intermittent self-catheterisation, gel reservoir catheters are the most cost effective.
Conclusions

- The use of different types of catheter for intermittent self-catheterisation is associated with slightly different rates of symptomatic UTI. Although some of these differences are statistically significant, all are associated with wide and overlapping confidence intervals, conferring uncertainty as to whether the effects are of clinical significance.

- Although gel reservoir catheters are the most effective type for intermittent self-catheterisation, they are associated with a cost of over £50000 per QALY: therefore, they are not considered cost effective.

- Clean non-coated catheterisation is the most cost effective method of intermittent self-catheterisation in 100% of model simulations. If clean non-coated catheters are not considered a relevant option, gel reservoir catheters are slightly more effective than hydrophilic with a small additional cost.
CONCLUSIONI

■ Quando trattare IVU
- Non trattare batteriuria-IVU asintomatiche
- Trattare se sintomi genitourinari e/o febbre, leucocitosi + urocoltura positiva (nell’anziano con demenza, in assenza di sintomi geniourinari, escludere sempre siti di infezioni alternativi)

■ Sintomi nel paziente anziano e disabile
- Considerare l’alterazione dello stato cognitivo-funzionale nell’anziano come indicativa di IVU solo se associata a urocoltura positiva e leucocitosi, escludendo altri possibili fattori eziologici

■ Che significato dare a stick urine
- La presenza di germi e nitriti nelle urine può supportare la probabilità di IVU, ma vi è un’alta prevalenza di falsi positivi/falsi negativi. Il trattamento antibiotico non andrebbe iniziato solo sulla base di questo dato in assenza di sintomi
- La piuria/leucocituria non è indicativa di per sè per batteriuria o IVU
CONCLUSIONI

- **IVU Health-associated**
  - E’ necessario riconoscere pazienti affetti da IVU acquisite in comunità ma Healthcare-Associated sulla base dei fattori di rischio, per definire prognosi e trattamenti più adeguati, al fine di evitare fallimenti terapeutici, maggior morbidità e mortalità

- **Adeguata gestione del catetere**
  - Usare il catetere vescicale sono nei casi strettamente necessari (interventi chirurgici localizzati in aree contigue al perineo, patologie ostruttive, pazienti critici)
  - Programmare con l’equipe infermieristica periodiche rivalutazioni all’uso del catetere vescicale
  - Non trattare batteriuria asintomatica neppure nei portatori di CV, eccetto nei pazienti sottoposti a interventi urologici