**Supplementary Results: Atypical symptoms in emergency department patients with urosepsis challenge current UTI management guidelines**

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**Table S1 Subject characteristics**

|  |  |  |
| --- | --- | --- |
|  | **All uroseptic patients**  n = 123 | **Random**  **non-septic patients**  n = 576 |
| **Demographics** | | |
| Age, median year (IQR) | 70 (61–82) | 56 (39–71) |
| Male, n (%) | 66 (54%) | 265 (46%) |
| Race/ethnicity |  |  |
| White non-Hispanic, n (%) | 106 (86%) | 425 (74%) |
| Asian | 8 (7%) | 21 (4%) |
| Unknown | 4 (3%) | 54 (9%) |
| Hispanic/Latino | 3 (2%) | 32 (6%) |
| Black or African American | 2 (2%) | 44 (8%) |
| **Triage information** | | |
| Temperature ≥ 100.4 at triage, n (%) | 28 (23%) | 8 (1%) |
| Heart rate, mean (sd) | 105 (28) | 87 (73-105) |
| Hypotension at triage (systolic blood pressure < 90 mm Hg), n (%) | 27 (22%) | 28 (5%) |
| Initial Glasgow Coma Scale < 15, n (%) | 36 (29%) | 101 (18%) |
| **Presenting symptoms** | | |
| Fever (reported or measured at triage) | 79 (64%) | 75 (13%) |
| Genitourinary symptoms | 40 (33%) | 45 (8%) |
| Atypical urosepsis presentation\* | 35 (28%) | 460 (80%) |
| **ED course** | | |
| Received vasopressors in ED within 24 hours, n (%) | 57 (46%) | 14 (2%) |
| Intubated in the ED, n (%) | 10 (8%) | 14 (2%) |
| SOFA score, median (IQR) | 6 (3–8) | - |
| **Outcomes** | | |
| Hospital mortality, n (%) | 16 (13%) | 28 (5%) |

\* We define atypical presentation at triage to include patients with no report of fever, no fever measured at triage, and no report of localizing GU symptoms. Of note, four (4) patients with atypical presentations developed fever in the ED after triage.

**Table S2 Symptoms of uroseptic patients**

|  |  |
| --- | --- |
| **Symptom** | **Uroseptic patients**  **N=123** |
| **At least one constitutional symptom, No. (%)** | 114 (93%) |
| Fevers/chills/rigors | 77 (63%) |
| Fatigue/malaise/weakness/lightheadedness/lethargy | 65 (53%) |
| Mental status changes | 50 (41%) |
| Body aches or myalgias | 6 (5%) |
| **At least one classic genitourinary (GU) symptom** | 38 (31%)\* |
| Abnormal (cloudy or bloody) urine | 12 (10%) |
| Dysuria | 12 (10%) |
| Back pain | 8 (7%) |
| Flank pain | 11 (9%) |
| GU pain | 1 (1%) |
| **At least one nonspecific symptom of major illness** | 74 (60%)\* |
| Nausea or vomiting | 39 (32%) |
| Abdominal pain\* | 36 (29%)\* |
| Shortness of breath | 18 (15%) |
| Headache | 9 (7%) |
| Focal neurological symptoms | 9 (7%) |
| Chest pain | 6 (5%) |
| **At least one confounding symptom** | 36 (29%) |
| Diarrhea | 21 (17%) |
| Dry or unspecified cough | 13 (11%) |
| Productive cough | 3 (2%) |
| Skin abnormalities (redness, swelling, or abscess) | 3 (2%) |
| Upper respiratory viral (sore throat, stuffy nose, or ear pain) | 5 (4%) |
| Extremity pain | 2 (2%) |

\* We did not categorize abdominal pain as a classic GU symptom. Only 6 of the 38 patients with “atypical symptoms” had any documented abdominal pain which was generally non-specific abdominal cramping or bloating. Additional details about symptoms of atypical urosepsis patients with abdominal pain are provided in the last five rows of Table S3 (“Detailed characterization of 35 urosepsis patients with atypical presentations”).

**Table S3 Detailed characterization of 35 urosepsis patients with atypical presentations (i.e., no GU localizing symptoms; no report of fever; and no fever at triage).**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Vignette | Malaise | Confusion | WBC  (L-1) | Lactate  (mmol/L) | Urine studies | UCx growth |
| 1 | 84M wheelchair-bound p/w 3d of lethargy, confusion | **+** | **+** | Arrow Up with solid fill  43.7 | Arrow Up with solid fill  4.2 | Pyuria on UA, >100 WBCs, BACT 3+, +LE | UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA COLI |
| 2 | 81M p/w SOB, ?STEMI, tachycardia | **+** | **–** | Arrow Up with solid fill  21.2 | Unk | Pyuria on UA, 20-50 WBCs, BACT 1+, +LE | No growth (Abx before UCx\*) |
| 3 | 55M w/ CRI on HD and recent bacteremia 2/2 urosepsis p/w hypoxia, SOB, HoTN | **–** | **–** | Arrow Up with solid fill  28.9 | Arrow Up with solid fill  1.8 | Pyuria on UA, >100 WBCs, BACT 3+, +LE | UCx grew moderate (10,000 to <100,000 CFU/ml) PSEUDOMONAS AERUGINOSA |
| 4 | 67F w/ neurogenic bladder, multiple prior UTIs p/w fatigue, weakness, hypoxia. Later found to have acute on chronic bladder obstruction. | **+** | **+** | Arrow Up with solid fill  16.0 | 0.9 | Pyuria on UA, >100 WBCs, BACT 1+, +LE | UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA COLI |
| 5 | 53M w/ quadriplegia in rehab facility p/w acute AMS | **–** | **+** | 7.6 | Arrow Up with solid fill  4.7 | Pyuria on UA, 50-100 WBCs, BACT 1+, +LE | UCx grew abundant (>=100,000 CFU/ml) KLEBSIELLA PNEUMONIAE |
| 6 | 72M w/ bacteremia, bladder CA (muscle invasive sarcomatoid carcinoma) s/p nephrostomy, HLD, AKI  p/w SOB. Later found to have complete R upper kidney obstruction | **+** | **–** | Arrow Up with solid fill  28.1 | Arrow Up with solid fill  9.0 | Pyuria on UA, 10-20 WBCs, +LE | (Abx before UCx\*) |
| 7 | 80M w/ artificial urethral sphincter p/w confusion | **+** | **+** | Arrow Up with solid fill  18.7 | Arrow Up with solid fill  5.3 | Pyuria on UA, 20-50 WBCs, +LE | (Abx before UCx\*)  UCx grew 100-1000 few E Coli by foley |
| 8 | 34F hx anaplastic astrocytoma s/p resection, VP shunt, XRT/chemo, prior long course of dexamethasone p/w inability to tolerate good PO, dizziness and nausea | **+** | **–** | 6.8 | Arrow Up with solid fill  7.7 | Pyuria on UA, >100 WBCs, BACT 1+ | (Abx before UCx\*)  UCx grew rare (100 to <1000 CFU/ml) gram negative rods |
| 9 | 82M w/ hx of Crohn’s, polyarteritis on digoxin found  unresponsive w/ asystolic arrest w/ episode of VT requiring ACLS x35 mins | **–** | **+** | Arrow Up with solid fill  15.2 | Arrow Up with solid fill  8.9 | Pyuria on UA, >100 WBCs, BACT 1+, +LE | UCx grew abundant (>=100,000 CFU/ml) CANDIDA ALBICANS |
| 10 | 85F w/ dementia, CVA, p/w hypotension, hypoxia. Later found to have 3mm stone with L hydronephrosis and L ureteral dilation | **–** | **+** | Arrow Up with solid fill  18.6 | Arrow Up with solid fill  5.1 | Pyuria on UA, >100 WBCs, BACT 3+, +LE | (Abx before UCx\*)  UCx grew Rare (100 to <1000 CFU/ml) ENTERIC GRAM NEGATIVE RODS. |
| 11 | 88M s/p partial pneumonectomy for pulmonary TB, left hemicolectomy w/ Hartmann's for diverticular bleed c/b parastomal hernia, recent surgery, recent UTI (on Bactrim) p/w confusion, fatigue | **+** | **+** | Arrow Up with solid fill  15.4 | Arrow Up with solid fill  16.3 | Pyuria on UA, 20-50 WBCs, BACT 1+, +LE | UCx grew abundant (>=100,000 CFU/ml) ENTEROCOCCUS |
| 12 | 56F h/o HTN p/w weakness and difficulty walking since last night | **+** | **–** | Arrow Up with solid fill  19.6 | Arrow Up with solid fill  4.6 |  | UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA COLI |
| 13 | 81M w/ CAD, CHF, HTN, AFib on coumadin, left hip fracture s/p ORIF p/w elevated creatinine, no complaints | **–** | **–** | Arrow Up with solid fill  31.8 | Arrow Up with solid fill  3.0 | Pyuria on UA, >100 WBCs, BACT 1+, +LE | UCx grew moderate (10,000 to <100,000 CFU/ml) KLEBSIELLA PNEUMONIAE |
| 14 | 48F h/o UTIs with E.coli ESBL and Candidia p/w weakness and fatigue. | **+** | **+** | Arrow Up with solid fill  50.6 | 0.9 | Pyuria on UA, >100 WBCs, BACT 2+, +LE | UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA COLI |
| 15 | 67M w/ dementia p/w AMS x2 days | **+** | **+** | Arrow Up with solid fill  21.4 | Arrow Up with solid fill  5.2 | Pyuria on UA, >100 WBCs, BACT 1+, +LE | UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA COLI |
| 16 | 81F PMH of pAF, EtOH use disorder, tachy-brady s/p PPM, HFpEF, HTN, HLD, COPD p/w weakness, n/d | **+** | **–** | Arrow Up with solid fill  18.1 | Arrow Up with solid fill  2.7 | Pyuria on UA, 20-50 WBCs, BACT 3+, +LE | UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA COLI |
| 17 | 62M w/ seizure disorder, adrenocortical insufficiency with resultant labile  sodium, R hemiparesis presents p/w SOB and CP. After initial presentation, developed fever | **+** | **–** | Arrow Up with solid fill  11.1 | Arrow Up with solid fill  2.5 | Pyuria on UA, 50-100 WBCs, BACT 3+ | (Abx before UCx\*)  UCx grew few (1000 to <10,000 CFU/ml) MIXED BACTERIA. |
| 18 | 86F w/ ESRD 2/2 DM p/w tachycardia and hypotension from HD | **–** | **–** | Arrow Up with solid fill  15.7 | Arrow Up with solid fill  4.9 | Pyuria on UA, >100 WBCs, BACT 3+, +LE | (Abx before UCx\*)  Abundant (>=100,000 CFU/ml) ESCHERICHIA COLI; |
| 19 | 76M w/ HTN, prostate CA (on chemo) p/w  weakness and diarrhea. Later found to be neutropenic. | **+** | **–** | Arrow Up with solid fill  0.3 | Arrow Up with solid fill  4.1 | No pyuria on UA, 5-10 WBCs | UCx grew abundant (>=100,000 CFU/ml) ENTEROCOCCUS |
| 20 | 50F w/ seizures and recurrent nephrolithiasis and UTIs s/p renal stents p/w unresponsiveness and tonic clonic shaking | **+** | **+** | Arrow Up with solid fill  13.6 | Arrow Up with solid fill  3.3 | Pyuria on UA, >100 WBCs, BACT 1+, +LE | No growth (Abx before UCx\*) |
| 21 | 79F w/ ESRD p/w AMS | **–** | **+** | Arrow Up with solid fill  17.0 | Arrow Up with solid fill  6.1 | Pyuria on UA, >100 WBCs, BACT 3+, +LE | UCx grew abundant (>=100,000 CFU/ml) YEAST (NOT CANDIDA ALBICANS)  Rare (100 to <1000 CFU/ml) PROBABLE ENTEROCOCCUS |
| 22 | 63F w/ ALS s/p trach, neurogenic bladder s/p suprapubic tube p/w hyperglycemia | **–** | **–** | Arrow Up with solid fill  16.2 | Arrow Up with solid fill  5.8 | Pyuria on UA, 20-50 WBCs, BACT 1+, +LE | UCx grew abundant (>=100,000 CFU/ml) SERRATIA MARCESCENS |
| 23 | 64M w/ MS p/w multiple falls | **–** | **–** | 9.1 | Arrow Up with solid fill  1.4 | Pyuria on UA, 20-50 WBCs, BACT 1+, +LE | (Abx before UCx\*)  UCx grew abundant (>=100,000 CFU/ml) ENTEROCOCCUS; Rare (100 to <1000 CFU/ml) MIXED BACTERIA.\*\* |
| 24 | 67M w/ SCI c/b paraplegia, neurogenic bladder s/p indwelling foley p/w unresponsiveness | **–** | **+** | Arrow Up with solid fill  13.7 | Arrow Up with solid fill  2.2 | Pyuria on UA, 10-20 WBCs, BACT 2+, +LE | UCx grew abundant (>=100,000 CFU/ml) MORGANELLA MORGANII  Abundant (>=100,000 CFU/ml) PROTEUS MIRABILIS |
| 25 | 86F w/ severe MR, DM, HTN, pulmonary HTN, AFib p/w confusion | **+** | **+** | Arrow Up with solid fill  12.1 | Arrow Up with solid fill  5.5 | Pyuria on UA, 20-50 WBCs, BACT 1+, +LE | UCx grew moderate (10,000 to <100,000 CFU/ml) ESCHERICHIA COLI; Abundant (>=100,000 CFU/ml) MIXED BACTERIA. |
| 26 | 84M w/ HTN, HLD p/w fall. After presentation, developed hypotension in the ED | **+** | **–** | Arrow Up with solid fill  36.5 | Arrow Up with solid fill  1.1 | Pyuria on UA, >100 WBCs, BACT 1+, +LE | UCx grew abundant (>=100,000 CFU/ml) ENTEROCOCCUS; Abundant (>=100,000 CFU/ml) MIXED BACTERIA WITH 1 POTENTIAL PATHOGEN IN RARE AMOUNT |
| 27 | 97yo man, PMH HTN, BPH and gout, who p/w increased weakness and confusion | **+** | **+** | 7.5 | Arrow Up with solid fill  1.6 | Pyuria on UA, >100 WBCs, BACT 3+, +LE | UCx grew moderate (10,000 to <100,000 CFU/ml) MIXED BACTERIA. |
| 28 | 75M w/ CKD on HD, CHF (EF 20%), p/w hypotension and AMS | **–** | **+** | Arrow Up with solid fill  17.1 | Arrow Up with solid fill  1.9 | Pyuria on UA, 20-50 WBCs, +LE | UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA |
| 29 | 80M p/w AMS | **–** | **+** | Arrow Up with solid fill  14.8 | Arrow Up with solid fill  1.7 | Pyuria on UA, 50-100 WBCs, BACT 3+, +LE | UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA COLI  Abundant (>=100,000 CFU/ml) ESCHERICHIA COLI of a second type |
| The following subjects with atypical presentations reported abdominal pain | | | | | | | |
| 30 | 83M w/ HTN, HLD, Asthma, s/p recent TURP p/w AMS and hypotension | **–** | **+** | Arrow Up with solid fill  21.7 | Arrow Up with solid fill  3.1 | Pyuria on UA, >100 WBCs, BACT 1+, +LE | UCx grew abundant (>=100,000 CFU/ml) ENTEROCOCCUS |
| 31 | 52F w/ short gut, Crohn’s ileostomy, bowel resections, frequent UTIs  p/w 2-3 days of worsening diffuse abdominal pain, dry heaves and diffuse body pain. | **–** | **–** | Arrow Up with solid fill  29.1 | 2.4 | Pyuria on UA, >100 WBCs, BACT 1+, +LE | Abundant (>=100,000 CFU/ml) KLEBSIELLA PNEUMONIAE |
| 32 | 85M w/ CAD, AFib, myasthenia gravis (on IMURAN), HLD, HTN, CKD (baseline Cr 1.48), DVT (on  coumadin) p/w LLQ abdominal pain. | **–** | **–** | 8.1 | 0.8 | Pyuria on UA, >100 WBCs, BACT 2+, +LE | UCx grew abundant (>=100,000 CFU/ml) KLEBSIELLA PNEUMONIAE, Abundant (>=100,000 CFU/ml) PSEUDOMONAS AERUGINOSA, Few (1000 to <10,000 CFU/ml) MIXED BACTERIA |
| 33 | 83M w/ head and neck cancer p/w coffee-ground emesis | **+** | **–** | Arrow Up with solid fill  15.8 | Arrow Up with solid fill  9.6 | Pyuria on UA, >100 WBCs, BACT 3+, +LE | UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA COLI, Abundant (>=100,000 CFU/ml) ESCHERICHIA COLI of a second type, Abundant (>=100,000 CFU/ml) STAPHYLOCOCCUS AUREUS |
| 34 | 60M w/ COPD, HTN, Hep C (not currently on meds) p/w watery diarrhea, nonbloody, no fever, mild abd  cramping. | **+** | **–** | Arrow Up with solid fill  23.1 | Arrow Up with solid fill  1.8 | Pyuria on UA, 50-100 WBCs, BACT 3+, +LE | UCx grew moderate (10,000 to <100,000 CFU/ml) NONHEMOLYTIC STREPTOCOCCUS |
| 35 | 55M w/ CVA and residual L sided weakness, schizphrenia, HTN, encephalopathy p/w  abdominal pain and distention x 1 week | **–** | **–** | Arrow Up with solid fill  21.1 | Arrow Up with solid fill  4.9 | Pyuria on UA, 50-100 WBCs, BACT 1+, +LE | Abundant (>=100,000 CFU/ml) PSEUDOMONAS AERUGINOSA, Abundant (>=100,000 CFU/ml) MUCOID PSEUDOMONAS AERUGINOSA |

**\*** Documented time of antibiotic administration was earlier than time of urinalysis collection documented in either the ED nursing notes or the lab specimen detail.

**Table S4 Triage SBP of 35 urosepsis patients with atypical presentations.**

|  |  |
| --- | --- |
| **Study ID** | **Triage SBP** |
| 1 | 77 |
| 2 | 65 |
| 3 | 131 |
| 4 | 141 |
| 5 | 71 |
| 6 | 126 |
| 7 | 76 |
| 8 | 70 |
| 9 | 30 |
| 10 | 90 |
| 11 | 113 |
| 12 | 125 |
| 13 | 88 |
| 14 | 84 |
| 15 | 136 |
| 16 | 95 |
| 17 | 97 |
| 18 | 93 |
| 19 | 158 |
| 20 | 76 |
| 21 | 103 |
| 22 | 158 |
| 23 | 140 |
| 24 | 102 |
| 25 | 126 |
| 26 | 129 |
| 27 | 120 |
| 28 | 80 |
| 29 | 142 |
| 30 | 52 |
| 31 | 111 |
| 32 | 115 |
| 33 | 105 |
| 34 | 136 |
| 35 | 118 |

**Table S5 Post-diagnostic pathologies of random, non-septic patients**

|  |  |  |
| --- | --- | --- |
| Any toxicological pathology | 96 | (17%) |
| Drugs of abuse | 78 | (14%) |
| Medication effect | 9 | (2%) |
| Withdrawal syndrome | 9 | (2%) |
| Any cardiac pathology | 88 (15%) | |
| Atrial fibrillation/SVT | 45 (8%) | |
| Other, including non-specific chest pain | 35 (6%) | |
| Any respiratory pathology | 72 (13%) | |
| CHF | 40 (7%) | |
| COPD/RAD | 24 (4%) | |
| Any neurological pathology | 68 (12%) | |
| Other neurological pathology | 45 (8%) | |
| Intracerebral hemorrhage | 12 (2%) | |
| Any gastrointestinal pathology | 61 (11%) | |
| Other, with no antibiotics | 34 (6%) | |
| GI bleed | 18 (3%) | |
| Any trauma pathology | 52 (9%) | |
| Fracture | 22 (4%) | |
| Other acute injury | 21 (4%) | |
| Any non-bacterial infectious disease | 26 (5%) | |
| Viral | 24 (4%) | |
| Fungal | 3 (1%) | |
| Any renal pathology | 22 (4%) | |
| Renal failure | 22 (4%) | |
| Any vascular pathology | 3 (1%) | |
| Aneurysm rupture | 3 (1%) | |
| Any other pathology | 171 (30%) | |