Improving antibiotic use for complicated urinary tract infections
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The additional value of blood cultures in patients with complicated urinary tract infections

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Abstract

We evaluated 800 hospitalized patients with a complicated urinary tract infection in whom on the day of start of antibiotic treatment both a blood- and a urine culture were obtained. In 70% of patients urine cultures were positive and blood cultures in 29%. In 7% of patients uropathogens caused bacteraemia with a pathogen that was not isolated from urine. Receiving antibiotic therapy at the moment of hospitalization was the only factor independently associated with discordant culture results (OR, 2.06; 95% CI, 1.18-3.61). For those receiving antibiotics at the moment of hospitalization blood cultures have additional diagnostic value over urine cultures.
Research Note

Bacteraemia is present in 15-25% of patients with complicated urinary tract infections (UTIs) [1]. In many UTI treatment guidelines collection of blood cultures is not recommended [2-4], as they may provide little additional diagnostic value over urine cultures [5-8]. In contrast, other authors recommend to collect blood cultures in all patients with a complicated UTI [9,10], or at least in patients at risk for discordant culture results, i.e. bacteraemia with uropathogens that could not be cultured from urine [11,12]. However, the risk factors for discordant culture results are not unambiguous [11,12]. The objective of the present study was to assess the rate of discordant culture results, and to identify for which group of patients collection of a blood culture seems useful.

We conducted a retrospective observational cohort study, which was part of the baseline measurement of a cluster-randomized trial testing a multifaceted antibiotic stewardship program in patients with a complicated UTI. Details have been described before [13]. Briefly, the departments of internal medicine and urology of 19 hospitals located throughout the Netherlands participated. Included were adult inpatients/outpatients diagnosed with a complicated UTI – including uncomplicated pyelonephritis - [13,14], who started with antibiotic therapy. For the present study, we only considered those hospitalized patients in whom both a blood culture and a urine culture were obtained on the day of start of antibiotic treatment. In case a patient was admitted after 9 PM, a urine culture of the next day was also accepted. The ethics committee deemed the study exempt from their approval.

Blood- and urine cultures were considered ‘positive’ when a bacterial pathogen was regarded as pathogenic (at least 10E4 or 10E5 cfu/ml) by the attending microbiologist and reported together with a susceptibility pattern. Contamination was defined as culture results that were regarded and reported as ‘contaminated’ by the attending microbiologist, or as a urine culture that revealed growth of at least 3 bacterial species. Coagulase-negative staphylococci isolated from a blood culture were also considered to represent contamination. Contaminated cultures were included in the analysis. A culture was defined ‘sterile’ when it did not show any bacterial growth or when a bacterial pathogen was regarded as low pathogenic by the attending microbiologist.

Concurrent blood- and urine cultures could be either discordant or concordant. A discordant culture result was defined as a positive blood culture with a related urine culture that showed growth of another microorganism, did not show bacterial growth, or was contaminated. In case of discordant culture results a blood culture was considered to have ‘additional value’ over a urine culture. A concordant culture result was defined as a positive urine culture with a related
Figure 1. Flowchart of patients

1,314 hospitalized patients with complicated UTI

Exclusion 494 patients:
- 239 patients only urine culture
- 160 patients only blood culture
- 93 patients no culture at all
- 2 patients missing data

820 patients providing blood- and urine culture

Exclusion 20 patients: missing culture results

800 patients with available blood- and urine culture result

- 743 patients with concordant culture result
- 57 patients with discordant culture result

- 16 patients: bacteraemia with different pathogen in urine culture
- 41 patients: bacteraemia without bacterial growth* in urine culture

* or with contamination
blood culture that showed growth of the same microorganism, showed no growth, or was contaminated. Concurrent sterile or contaminated blood- and urine culture results were considered ‘concordant’ as well. In case of concordant culture results a blood culture was considered to have ‘no additional value’.

Of 1,314 patients with a complicated UTI, 514 were excluded, mainly because blood and/or urine cultures had not been performed, but 800 were included (Figure 1). Baseline characteristics are listed in Table 1.

The urine culture results showed one pathogen in 492 and two pathogens in 71 patients, accounting for 70% (563/800) positive urine cultures. *Escherichia coli* (as single pathogen) was the most common pathogen in positive urine cultures (63%, 355/563), followed by *Klebsiella* species (7%, 39/563). *Staphylococcus* species was cultured in 9 patients (2%), namely *Staphylococcus aureus* (1%, 8/563) and *Staphylococcus saprophyticus* (0.2%, 1/563). Additionally, 2% contaminated (13/800) and 28% sterile urine cultures (224/800) were obtained.

The blood culture results showed one pathogen in 224 and two pathogens in 5 patients, accounting for 29% (229/800) cultures revealing bacteraemia. *E. coli* (as single pathogen) was cultured in 72% (164/229) and *Klebsiella* species in 7% (17/229). *Staphylococcus* species was cultured in 10 patients: *S. aureus* in 1% (3/229) and Coagulase-negative staphylococci in 7 patients, which were considered as contamination. Contaminated and sterile blood cultures were obtained in 3% (21/800) and 69% (550/800), respectively.

Overall, 7% (57/800) of the patients had discordant culture results. Of these patients 28% (16/57) had a different bacterial species in the blood culture compared to the related urine culture, whereas 72% (41/57) had bacteraemia with a related urine culture showing contamination or no bacterial growth (Figure 1).

Potential risk factors (uni- and multivariate) for discordant culture results are shown in Table 1. Blood cultures were more often sterile in pretreated compared to non-pretreated patients (74% versus 65%; p=0.01). Covariates associated with discordant culture results on univariate analysis at a level of significance of P< 0.2 were included in a multiple logistic regression model using a forward procedure. Receiving antibiotic therapy at the moment of presentation was the only factor independently associated with discordant culture results (OR, 2.06; 95%CI, 1.18-3.61). Receiving antimicrobial treatment at the moment of presentation was associated with a 10.1% risk of having discordant culture results, compared to 5.4% without antimicrobial treatment (risk difference, 4.7%, 95% CI 0.91-9.1%).

Summarizing, in 7% of patients uropathogens caused bacteraemia with a pathogen that was not isolated from the urine. Receiving antibiotic therapy at
Table 1. Baseline characteristics and risk factors for discordant blood culture results for 800 patients with complicated UTI *

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=800)</th>
<th>Concordant (n=743)</th>
<th>Discordant (n=57)</th>
<th>Univariate OR (95% CI)</th>
<th>P</th>
<th>Multivariate OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>63.5 (21.2)</td>
<td>63.1 (21.3)</td>
<td>67.9 (19.5)</td>
<td>1.13 (0.98-1.29)</td>
<td>0.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>339 (42)</td>
<td>314 (42)</td>
<td>25 (44)</td>
<td>1.07 (0.62-1.84)</td>
<td>0.81</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Febrile UTIb</td>
<td>714 (89)</td>
<td>662 (89)</td>
<td>52 (91)</td>
<td>1.59 (0.56-4.51)</td>
<td>0.38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anyc</td>
<td>498 (62)</td>
<td>461 (62)</td>
<td>37 (65)</td>
<td>1.13 (0.64-1.99)</td>
<td>0.67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>183 (23)</td>
<td>170 (23)</td>
<td>13 (23)</td>
<td>1.00 (0.52-1.89)</td>
<td>0.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>95 (12)</td>
<td>89 (12)</td>
<td>6 (10)</td>
<td>0.87 (0.36-2.07)</td>
<td>0.74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urological comorbidity</td>
<td>173 (22)</td>
<td>157 (21)</td>
<td>16 (28)</td>
<td>1.46 (0.80-2.67)</td>
<td>0.22</td>
<td></td>
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<tr>
<td>Urinary catheter</td>
<td>150 (19)</td>
<td>138 (19)</td>
<td>12 (21)</td>
<td>1.17 (0.60-2.27)</td>
<td>0.64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotic therapy within past 14 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- No</td>
<td>462 (58)</td>
<td>437 (59)</td>
<td>25 (44)</td>
<td>Reference</td>
<td>0.05</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>- Yes, but finished course</td>
<td>51 (6)</td>
<td>48 (6)</td>
<td>3 (5)</td>
<td>1.09 (0.32-3.75)</td>
<td>0.89</td>
<td>1.09 (0.32-3.76)</td>
<td>0.89</td>
</tr>
<tr>
<td>- Antibiotics at the moment</td>
<td>286 (36)</td>
<td>257 (35)</td>
<td>29 (51)</td>
<td>1.97 (1.13-3.44)</td>
<td>0.02</td>
<td>2.06 (1.18-3.61)</td>
<td>0.01</td>
</tr>
<tr>
<td>Internal medicine ward</td>
<td>615 (77)</td>
<td>567 (76)</td>
<td>48 (84)</td>
<td>1.66 (0.80-3.44)</td>
<td>0.17</td>
<td></td>
<td></td>
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<tr>
<td>(compared to Urology ward)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>University hospital</td>
<td>209 (26)</td>
<td>196 (26)</td>
<td>13 (23)</td>
<td>0.83 (0.44-1.56)</td>
<td>0.55</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* missing data in < 2 patients; numbers are n (%), unless otherwise indicated

a OR per 10 years increase in age (per 1 year increase in age: OR 1.01; 95% CI: 1.00-1.03)
b Febrile UTI included (uncomplicated) pyelonephritis, urosepsis, acute prostatitis and UTI with systemic symptoms, defined as fever (temperature ≥ 38°C), haemodynamic instability or delirium.
c Comorbidity included one or more of the following diseases: cardiovascular disease, immunocompromising disease (HIV, cancer for which chemotherapy within last 3 months, or immunocompromising medication (e.g. prednisone, methotrexate, azathioprine, TNF-alpha blocker)), diabetes mellitus, urological comorbidity (an anatomical abnormality of the urinary tract (excluding benign prostatic hyperplasia), a history of urolithiasis, or neurological urinary retention), and kidney disease.
d Overall Wald test
e Multivariate OR obtained by forward regression analysis and selecting variables with P<0.2 in univariate analysis as independent covariate
f Overall P-value
the moment of presentation doubled the risk for the presence of discordant culture results.

To our knowledge, our study has the largest sample size and is the first to evaluate the total, diverse population of patients with complicated UTIs. Present antibiotic therapy turned out to be the only independent risk factor, which confirmed results of Van Nieuwkoop et al. [12], but disagreed with Etienne et al., who found that blood cultures were always sterile in pretreated patients [11]. Oral antibiotic UTI treatment may be able to sterilize the urine, as for many antibiotics concentrations in the urine are high, while having an insufficient antimicrobial effect at the blood level, with a resulting positive blood culture [12].

A limitation of our study is its retrospective design, and we only included patients with a complicated UTI in whom both urine- and blood cultures had been performed. Another limitation can be the inclusion criterium that blood and urine had to be taken at the day of starting treatment. We accepted for patients admitted after 9 PM also urine cultures of the next day, because taking a urine culture can be delayed by waiting for voiding, or catheterization. Nevertheless, this scenario represents clinical practice, making the percentages we found still clinically relevant.

Our observed rate of 7% discordant results was relatively high, compared to the rates varying between 0-5% in other, mostly retrospective, studies in adult, non-pregnant patients with a UTI. However, these studies were performed in subgroups of patients [5-8,11,12]. Two studies showing a rate of discordant results of 5% also included patients that received antimicrobial pretreatment, but in one study only men with acute prostatitis were evaluated [11] and in the other only patients with a febrile UTI [12].

We recommend collecting both blood- and urine cultures in patients who receive antibiotics at the moment of hospitalization, because this appears to have a clear added diagnostic value. It remains to be discussed whether taking blood cultures in the other patients with complicated UTIs is warranted.
References


