Linking Process Measures to Outcome for Patients With Complicated Urinary Tract Infection: It’s Complicated

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(See the Major Article by Spoorenberg et al on pages 164–9.)

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Defining best practice and measuring compliance with standards for the management of infection is challenging. Quality indicators (QIs), many of which measure process, are being increasingly developed to address these challenges [1–4], in some cases using a “bundle” approach where compliance is measured as “all or nothing” [5]. One could argue that these process measures end up measuring what can be measured rather than what should be measured [6]. It is therefore desirable to define clinical outcome measures that are sensitive to changes in the quality of care, for example to increased compliance with QIs. This presents significant challenges, but demonstrating links between process and outcome is necessary to convince clinicians and allow more meaningful external scrutiny [6]. Mortality, defined in a number of ways, is one of the most objective clinical outcome measures, but its application where an infection is associated with a low mortality rate, such as urinary tract infection (UTI), is limited. Very large sample sizes are required to demonstrate any significant changes and there is likely to be significant confounding by indication (the sickest patients who receive the best care are still most likely to die). Length of hospital stay (LOS), a continuous variable applicable to all patients, should theoretically be more sensitive to changes in practice. Although subject to numerous confounders, significant associations between increased guideline adherence and decreased LOS have been demonstrated in community-acquired pneumonia [7].

In this issue of Clinical Infectious Diseases, Spoorenberg and colleagues [8] report the findings of a large retrospective observational multicenter cohort study to evaluate whether adherence to a set of QIs defining appropriate antibiotic management for patients with complicated UTI was associated with LOS, the primary outcome measure. The 4 QIs were as follows: (1) perform a urine culture before starting treatment; (2) prescribe empirical treatment in accordance with the national guideline (2B only) and have been previously validated [1]. Using multilevel analysis is appropriate because discharge practices will differ by department and hospital independent of patient characteristics. However, the statistical analysis of LOS is often difficult due to nonnormal distribution, habitually including many outliers, [9] and it is not clear whether this was considered in the statistical modeling. Several other limitations also affect the interpretation and generalizability of the study findings. In all retrospective studies, case ascertainment bias is an important potential threat,
exemplified here where the method of case identification is not given, making the completeness of case ascertainment impossible to assess. Furthermore, the justification for some of the study inclusion and exclusion criteria is unclear. The “nonfebrile complicated UTI” group includes UTI without systemic symptoms in catheterized patients. This appears to include patients with asymptomatic bacteruria (an inevitable consequence of long-term catheterization [10]), which should not be considered complicated UTI. Conversely, the study excluded patients with UTI with a nephrostomy or after a urological procedure on the grounds that the Dutch national guideline does include treatment recommendations for these infections, so prescribing in accordance with national guidelines (the second QI) could not be applied. However, it is reported that the “national guideline contains a general recommendation for patients with a complicated UTI” [8]. It may have been the case that this general recommendation and/or prescribing in accordance with local guidelines (indicator 2B) could have been applied to these patients instead. Furthermore, many other patients who were included in the study did not qualify for all 4 QIs, so the exclusion of this important group seems unjustified, even if 1 of the QIs was inapplicable, and it limits the generalizability of the study findings.

The first QI was generously inclusive, with urine cultures sent the following day for patients admitted after 9 PM qualifying as “performed before starting treatment” [8]. Patients with sepsis and/or complicated UTI should receive prompt antibiotic therapy [1, 3], so cultures sent the following day should not be before treatment. Treatment delays to allow prior cultures should be avoided but the QI definition should be tight (eg, patients admitted after 9 PM should not be included in that QI if there is no chance of adherence). Splitting the second QI into 2 indicators, measuring accordance with local and national guidelines separately, hinders useful interpretation. The only reason to analyze these separately would be to demonstrate superiority of one kind of guideline, but this is not discussed. It might be interesting to briefly discuss instances of adherence with local but not national guidelines or vice versa, but the QI should be adherence with the national or local guideline. The reported statistically significant reduction in LOS associated with adherence to local, but not to national, guidelines is unhelpful in the absence of illness severity data. The report states that local guidelines tend to include selected options from a range of options offered in the national guideline. It is highly plausible that prescribers would prefer to select specific antibiotics for very sick patients, whether in accordance with local policy or not, whereas they are more likely to be compliant with local guidelines for the less sick patients. This confounds the reported association between adherence to local guidelines and reduced LOS by potentially selecting the less sick or complicated patients.

The intravenous to oral switch indicator was limited by the small proportion (<50%) of patients who met the relevant criteria. Even among these, there was a clinically and statistically significant reduction in LOS associated with early intravenous to oral switch, which is not surprising and may be due to practicality rather than faster recovery. Either way, early intravenous to oral switch in clinically stable patients should be advocated, in the absence of specific infections mandating intravenous therapy [11]. The fourth QI, tailoring antibiotic therapy according to culture results, is important, although it was not associated with LOS in this study. Tailoring aims to reduce the selection of resistant organisms and reduce the risk of *Clostridium difficile* infection, so is unlikely to directly impact significantly on the LOS of the index admission. Classification of fluoroquinolones as a narrow-spectrum agent in this context is inappropriate, although a suitable choice of agent in the absence of other oral options.

The multilevel approach, accounting for within-department and hospital similarities, is appropriate, but the inclusion and exclusion of some variables in the adjusted models are not justified. The value of “urological comorbidity” as an additional variable when all the patients have complicated UTI is not clear. The selection of “other comorbidities,” and how these were categorized and/or weighted, should be explicit. Measuring and adjusting for comorbidity is complex, so use of a validated score aids interpretation [12]. The inclusion of an illness severity score is also essential to make any judgement about associations between process and outcome. This study reports that there is “no scoring severity system specific for UTI patients” but generic sepsis definitions can be applied to infections from any source [13]. The study definitions of febrile vs nonfebrile UTI do not deal adequately with this issue.

Most importantly, this study reports a reduction in LOS associated with increasing proportional adherence to applicable QIs, which is the key purpose of having a set of QIs. Some indicators in isolation, for example, performing a urine culture, will not influence LOS but could contribute to a set of QIs that might reduce LOS when performed in combination. However, this study does not fully report the proportional QI adherence. Although the numbers in each tertile of proportional adherence to the QI, and the numbers of patients qualifying for each QI separately, are given, the total numbers of patients qualifying for 1, 2, 3, or all 4 of the QIs are required to aid interpretation. It is also not clear how prescribing in accordance with local and national guidelines was dealt with in this analysis. Last, the numbers of patients meeting secondary outcome measures were too small to make any meaningful conclusions. The observation that concordance with local guidelines was associated with fewer admissions to ICU is probably confounded in the same way as the association with LOS.
In conclusion, this study is a bold and valuable attempt to link process and outcome measures among patients with complicated UTI. It applied a set of 4 validated QIs in a retrospective cohort study using appropriate statistical methods, but the limitations affect the interpretation and generalizability of the findings. These limitations reflect the difficulties in demonstrating links between quality of care and clinical outcomes—it’s complicated.

**Note**

_Potential conflicts of interest._ Both authors: No reported conflicts.

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