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Procalcitonin, pyuria and proadrenomedullin in the management of Urinary Tract Infections - the 'Triple P in UTI' study: Optimal patient transfer in the canton of Argovia [Optimaler Patiententransfer im Kanton Aaragau] (OPTIMA III)

Submission date	Recruitment status	[_] Prospectively registered
22/05/2012	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
03/07/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
06/05/2015	Urological and Genital Diseases	

Plain English summary of protocol

Background and study aims
Urinary tract infections (UTIs) are among the most common infectious diseases and are responsible for hospitalization and antibiotic overuse. An early and adequate risk assessment improves patient care and the appropriate use of limited healthcare resources. Antibiotic overuse leads to antibiotic resistance, which is a marker for poor outcome. The blood biomarkers procalcitonin (PCT) and proadrenomedullin (ProADM) are effective and useful to guide antibiotic treatment and prognostic assessment in patients with other infections. The aims of this study are to compare the performance of treatment and management based on the standard guidelines with antibiotic treatment guided by the biomarker PCT and site-of-care decisions guided by the biomarker ProADM.

Who can participate?
All adult patients (18 years of age or older) with UTI presenting to the emergency department at the Kantonsspital Aarau, Switzerland.

What does the study involve?
Patients will be randomly assigned into two groups regarding antibiotic treatment and, independently, into two groups regarding site-of-care decisions. Duration of antibiotic treatment will be based on the standard guidelines (control group) or guided by the biomarker PCT and urine leukocyte counts (PCT-Pyuria group). Site of care will be recommended based on risk with ProADM (ProADM group) or without ProADM (control group). The possible sites of care are hospital or intensive care for those with high risk, and ambulatory post-acute care (home health care, health resort, rehabilitation or nurse-led care) for those with low risk. We will evaluate patients at discharge from hospital, 30 and 90 days after admission. Blood samples are

collected on admission and on day 3, and every other day while a patient receives antibiotics. Urine will be collected on admission and on day 3 after enrollment, 7 days after the end of treatment, on day 30 after enrollment and in case of clinical recurrence within 90 days. Telephone interviews will be performed on day 30 and day 90.

What are the possible benefits and risks of participating?
The risks are considered low. The main risks involve blood loss from taking blood, early stopping of antibiotics and early discharge from the hospital. We try to minimize all potential risks. Benefits of participation are in relation to possibly fewer antibiotic side effects and a lower risk of hospital-associated complications.

When is the study starting and how long is it expected to run for?
The study started in April 2012 and will run until February 2014.

Who is funding the study?
Funds of the Kanton Aargau, Switzerland and the hospital research fund of the Kantonsspital Aarau.

Who is the main contact?
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Study website
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Procalcitonin, Pyuria and Proadrenomedullin in the management of urinary tract infections - the 'Triple P in UTI' study (OPTIMA III): a trial using a factorial design of two randomized controlled intervention studies

Acronym
Triple P in UTI / OPTIMA III UTI

Study objectives
1. PCT-and pyuria-guidance reduces antibiotic exposure by 2 days (8 days versus 10 days in the control group)
2. ProADM-guided triage reduces physician-led length of stay in the index hospitalization by 1.5 days (4.5 days versus 6 days in the control group)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Canton of Aargau Ethics Committee, 29/03/2012, ref: EK 2012/010

Study design
Factorial design of two randomized controlled intervention studies

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Urinary Tract Infection (UTI)

Interventions
Duration of antibiotic therapy will be based on guidelines (control group) or guided by diagnosis-specific PCT and pyuria cut-off ranges (PCT-Pyuria group).

All patients will receive a guideline-based, multidisciplinary care bundle, enforced with high intensity and including clinical (medical stability), biopsychosocial and functional scores, and structured discharge planning considering patient's preferences and current living situation.

Site of care will be recommended risk-based with ProADM (ProADM group) or without (control group) on days 0 and 3:
1. High risk: hospital or intensive care
2. Low risk: ambulatory care, post-peracute care (home health care, health resort, rehabilitation) or nurse led unit/care (NLU/NLC).

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. Duration of antibiotic therapy (Antibiotic therapy study)
2. Physician-led length of stay during the index hospital exposure (triage study)

Secondary outcome measures
1. Analyzing the efficacy and safety of a PCT- and pyuria-guided antibiotic therapy to individualize and reduce antibiotic duration compared to guidelines.
1.1 Clinical and microbiological cure 7 days after end of therapy
1.2 30 day rate of clinical and microbiological recurrence
1.3 90 day rate of clinical recurrence
1.4 Antibiotic associated side effects
1.5 Relationship of pyuria, urine culture cut-offs and urinary á1-microglobulin/creatinine ratio with presence of pyelonephritis and level of biomarkers (CRP, PCT, ProADM, and other biomarkers such as urea, natriuretic peptides (ANP, BNP), copeptin, endothelin, apoprotein A1).
1.6 Correlation between sonographic signs of pyelonephritis and diagnosis based on urine culture cut-offs, clinical criteria and biomarkers.
2. Testing the impact of ProADM-enhanced triage decisions compared to standard of care, both in high-intensity implementation of interdisciplinary risk assessment for triage in patients with UTIs presenting to an ED on length of stay, regarding:
2.1. Other measures of resource utilization (different definitions of length of stay including rehospitalisation; treatment changes)
2.2. Adherence to triage algorithms
2.3. Functional status and adverse events (i.e. mortality; rate of complications)
2.4. Patient satisfaction
2.5. Quality of life assessment
2.6. Effective and chargeable costs for treatment path.
Endpoints will be assessed at discharge to non-hospital setting, 30 days and 90 days after admission.

Overall study start date
12/04/2012

Completion date
28/02/2014

Eligibility

Key inclusion criteria
1. Patients 18 years of age or older
2. Admitted from the community or a nursing home with acute (i.e. symptoms less than 28 days) UTI as one main diagnosis based on at least one clinical symptom (core body temperature >= 38.0° C, urgency, frequency of micturition, dysuria, suprapubic pain, flank pain, costovertebral angle tenderness, nausea and vomiting)
3. One urinary criterion (pyuria (>20 leukocytes/µl), and/or nitrites) in patients without antibiotic pretreatment. If the initial and final diagnoses are discrepant, the patient will be classified according to the final diagnosis. If the final diagnosis is different from an UTI, the patient will be classified as others.
4. Ability to understand verbal and written instructions and informed consent by patient or available relatives. If both the patient is unable to provide informed consent (e.g. dementia, coma) and there are no relatives available, an independent physician, who is not involved in the trial, may provide the informed consent based on the presumed will of the patient.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
300

Key exclusion criteria
1. Pregnancy
2. Immundeficiency (neutrophiles <500/ìL; if HIV+: CD4<350/ìL, leukemia, lymphoma, myeloma, cytotoxic medications, hemodialysis, transplant patients)
3. Prostatitis (i.e. increased PSA-level >4, or PSA more than double of a pre-existing baseline level, or pain on palpation)
4. Implanted foreign bodies in the urinary tract or urinary catheters
5. Patients with endovascular prostheses or foreign bodies
6. Patients with non-endovascular prostheses or foreign bodies within 6 months after implantation
7. Pre-treatment with antibiotics within the last 48 hours
8. Patients without command of the German (or other local) language, who will not be able within reason to get translation (e.g. family members) during admission, hospitalization and follow-up telephone interview
9. Terminal and very severe disease or medical co-morbidity where death is imminent and comfort therapy is provided
10. Foreseeable non-compliance for follow-up (e.g. current drug abuse)

Date of first enrolment

12/04/2012

Date of final enrolment
28/02/2014

Locations

Countries of recruitment
Switzerland

Study participating centre
Kantonsspital Aarau
Aarau
Switzerland
5001

Sponsor information

Organisation
Kantonsspital Aarau (Switzerland)

Sponsor details
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Sponsor type
Hospital/treatment centre

Website
http://www.ksa.ch/1440.asp

ROR
https://ror.org/056tb3809

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Kantonsspital Aarau (Switzerland)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	22/03/2013		Yes	No
Results article	results	01/05/2015		Yes	No