Microorganisms attached to the lumens and balloons of indwelling urinary catheters and correlation with symptoms, antibiotic use, and catheter specimen of urine results

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Abstract:

Purpose: To quantify and identify microorganisms attached to the lumens and balloons of removed urethral urinary catheters and relate this to patient-specific information.

Methodology: Indwelling urethral urinary catheters were collected from patients at a large teaching hospital in the UK. The balloon and lumen were separated, sonicated, and microorganisms were enumerated from the sonicate. Catheter specimen urine results were retrospectively reviewed.

Results: Sixty-one catheters were analysed. The most commonly isolated organisms were *Escherichia coli* and *Enterococcus faecalis*. 19.7% of patients received antibiotics while catheterised and 25% of those had a multi-drug resistant (MDR) organism attached to the lumen. Conversely, only 2.04% of catheters from patients not known to be receiving antibiotics had a MDR organism present. All lumens were colonised irrespective of antibiotic use. Symptom presentation did not correlate with numbers of colonising organisms or species. Despite heavy colonisation, only 8/61 patients were symptomatic.

Conclusion: This study demonstrated that indwelling urinary catheters in place for 10 days or greater were universally colonised and there was no correlation of colonisation with symptom presentation. Symptomatic presentation remains for the most important factor for defining CAUTI.

Introduction:

Infection is a well-recognised and costly complication of use of indwelling urinary catheters and is associated with increased mortality and increased length of hospital

stay(1, 2). The common causative agents of CAUTI reported in the USA include *Escherichia coli*, *Klebsiella pneumoniae*, *Enterococcus* spp., *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Candida* spp., and staphylococci(3) with approximately 20% of organisms isolated being multidrug-resistant (MDR)(4).

However, there has been considerable confusion between symptomatic UTI (CAUTI) requiring antibiotic treatment and asymptomatic bacteriuria (CAASB) found commonly in catheterised patients but not requiring treatment. This has led to over-use of antibiotics with concomitant concern regarding resistance and adverse events (5). Most of the data on causative bacteria of both CAUTI and CAASB are derived from urine samples taken from the catheter (despite these being discouraged in catheterised patients) and little is known about the bacteria that colonise catheters(6). Though some authors have examined catheters, there has not, to our knowledge, been a systematic, quantitative study of the contents of removed urinary catheters. Therefore, this pragmatic study aims to quantify organisms attached the lumens and balloons of indwelling urethral urinary catheters and correlate this with patient data on antibiotic usage, symptom presentation, and catheter specimen urine (CSU) results.

Methods:

Setting and sample collection

Between June 2015 and July 2016, indwelling urethral urinary catheters that remained in situ for ten days or greater from male and female patients over 16 years of age were collected from patients at Nottingham University Hospitals NHS Trust, Nottingham, UK. Catheters were collected from urology theatres, male urology ward, neurosurgery wards, and a neurorehabilitation centre by clinical staff when removed according to clinical need. Clinical staff were instructed to remove the catheter according to standard local protocols and if possible drain, but not flush, the lumen of any residual urine. Clinical staff were provided with an audit form to complete with patient details including the date the catheter was inserted, if the patient was prescribed antibiotics to their knowledge, and if they were symptomatic for CAUTI. Catheters were collected from

areas where experienced ward staff were familiar with CAUTI and its diagnosis. Local guidelines state antibiotics for CAUTI should be started immediately and the catheter changed during the treatment course, which is 7 days. The catheters were then placed in a resealable bag and stored in the specimen fridge (approx. +4°C) with information about antibiotics received and current symptoms of CAUTI. The catheters were analysed within 24 hours of removal.

An audit to retrospectively review catheter specimen urine (CSU) results during the period of catheterisation of the patients who had catheters included in this study was approved by Nottingham University Hospitals NHS Trust (Audit ID: 17-309Q) in December 2017. The period of catheterisation was available in the notes and according to the audit form provided by the clinical staff. All CSU results from each patient's period of catheterisation with the collected catheter were obtained retrospectively from microbiology reports available on a hospital-wide information system, NotIS (Nottingham Information System).

Analysis of catheters

The catheter was removed from the specimen bag using sterile forceps and placed onto a sheet of sterile autoclaved aluminium foil. Stainless steel, straight-jawed surgical clamps clamped the catheter on the lumen downstream of the balloon and on the lumen upstream of the drainage and balloon inflation ports. The balloon was then detached from the catheter body using a sterile scalpel and placed into a sterile universal container. Phosphate buffered saline (PBS, Oxoid, Basingstoke, UK) was added to the Universal container so that it covered the entire surface of the balloon section. The drainage and balloon inflation ports were separated from the catheter body and discarded. This left the lumen section with its ends clamped. Opening both ends of the clamps briefly, 1-2 mL PBS were introduced to fill the lumen depending on the size of the catheter. The ends were quickly reclamped and the catheter placed into a resealable freezer bag.

The balloon section and catheter lumen were sonicated for five minutes at 30 kHz to detach microorganisms. After sonication, both ends of the catheter body section were cleaned with an alcohol pre-injection swab (Mölnlycke Healthcare, Göteborg, Sweden). The lumen sonicate was drained into a sterile Bijou bottle (Sterilin, Newport, UK). 200µL of the balloon and lumen sonicates and appropriate dilutions were spread onto cysteine-lactose electrolyte deficient (CLED) agar (Oxoid, Basingstoke, UK) and incubated overnight in air at 37°C. Colonies were enumerated and general microbiological identification performed, including use of the API identification system (bioMérieux, Marcy-l'Étoile, France) and MALDI-ToF (Microflex LT Mass Spectrometer, Bruker Daltronics). All isolates were tested for resistance according to EUCAST guidelines(7, 8). If culture negative, the plates were incubated for a further 24 hours.

Statistics

Data were analysed in GraphPad Prism 7.01 (La Jolla, California, USA). Normality was assessed by histogram, and some data not normally distributed were log-transformed. Correlation was assessed using the Pearson correlation. Significance was defined as $p<0.05$ and was calculated by unpaired t-test and one-way ANOVA depending on the number of comparisons.

Results:

Catheter Collection Demographics

Sixty-one urethral urinary catheters were analysed. The mean age of patients from who the catheters were collected from was 68 years and 10/61 were female. The reasons for catheterisation were predominantly for management of urinary retention (64.62%), management of neurological or neurosurgical issues (21.31%), and transurethral resection of the prostate (16.39%), which correspond with specialties of the departments from which they originated. The types of catheters also varied with the majority being all-silicone for long-term use (50.8%), PTFE-coated (23.33%), all-silicone for short-term use (15.00%), latex (3.33%), hydrogel-coated latex (3.3.3%), and

hydrogel-coated silicone (3.33%). There was no significant difference in the quantity (p=0.4803, one-way ANOVA) of organisms attached to lumens of the different catheter types. However, there were more species of microorganisms per catheter attached to PTFE catheters than to all-silicone catheters (p=0.0073). The lumen sizes ranged from 12Ch to 20Ch.

Identification of microorganisms attached to the lumens and balloons

107 and 103 organisms were isolated from the lumens and balloons, respectively, of 58 urinary catheters. Three lumens (4.9%) and three balloons (4.9%), not from the same catheter, were culture - negative. The same microorganisms were isolated from the lumen and the balloon of the same catheter in 65.6% of collected catheters. The most commonly isolated organisms in both the balloons and lumens were *E. coli* and *E. faecalis* (Table I).

Drug Resistance and Antibiotic Exposure

Sixteen urinary catheters (26.2%) were from patients known to be receiving antibiotics and 12 of these were known to be receiving antibiotics for treatment of CAUTI, the other four receiving antibiotics prophylactically for other conditions and for treatment of other infections. Antibiotics prescribed for treatment of CAUTI included iv piperacillin-tazobactam, amoxicillin clavulanic acid, trimethoprim and pivmecillinam. Antibiotics for the four receiving antibiotics prophylactically and for other infections include iv piperacillin-tazobactam, amoxicillin clavulanic acid, vancomycin and meropenem. Of the 16 catheters from patients known to be receiving antibiotics, all lumens were colonised by at least one microorganism and 15/16 of the balloons were colonised. Antibiotics did not significantly reduce colonisation of catheter lumens (p=0.7153) or balloons (p=0.4516).

Four multi-drug resistant organisms were isolated, including two extended-spectrum beta-lactamases (ESBL)-producing *E. coli* and two meticillin-resistant *S. epidermidis.* MDR organisms were isolated from 25% of catheters from patients known

to be receiving antibiotics and from 2.04% of catheters from patients not known to be receiving antibiotics (p=0.0216, Fisher's exact test).

Length of catheterisation and colonisation of catheter lumens

Information regarding the exact duration of catheterisation was available for 48/61 catheters. There was no correlation between the duration of catheterisation and the number of microorganism species (Figure 1a) or the quantity of each microorganism (Figure 1b) in the lumen for catheters from patients symptomatic for CAUTI and asymptomatic. 8/61 patients were symptomatic for CAUTI (despite 12 being treated for CAUTI, only 8 had symptoms recorded) and length of catheterisation was available for 7/8. There was no significant difference between the number of isolates (p=0.7741) or the quantity (CFU/mL) (p=0.0976) of microorganisms isolated from the lumens of catheters from symptomatic and asymptomatic patients underlining the importance of symptoms, not microbiological culture, in the diagnosis of CAUTI.

CSU and Catheter Colonisation

Three of the 61 patient notes were unavailable and were not included in this analysis. 28 CSU samples from 22 patients were taken during the period of catheterisation from which the catheter was collected and processed as standard by the microbiology department. Generally, there was a poor consensus between the laboratory CSU results and the organisms attached to the catheter lumens and balloons in that additional organisms (the majority of which were *E. faecalis*) were excluded from the reports despite catheter colonisation in significant numbers. Only 28.6% of the laboratory CSU reports matched the contents of the lumen and balloon. This suggests that CSU results do not reflect what is present on the catheter.

Antibiotic choice does not appear to be influenced by CSU results. Two of the 12 patients prescribed antibiotics for CAUTI never had a CSU sent, and an additional 2/12 had a CSU sent but the results were 'no growth'. An additional patient was prescribed

cephalexin for an ESBL *E. coli* and another patient was prescribed pivmecillinam despite the results of a pivmecillinam resistant *Proteus spp*. in the report.

Discussion:

A novel method was developed for analysing the attached bacteria in the lumens and balloons separately without sampling the catheter external surface. The most commonly isolated organisms from the lumens and balloons of indwelling urinary catheters were Enterobacteriaceae and enterococci. Of interest, *Proteus mirabilis* is frequently cited (9) as a major problem in catheter users, but was isolated from only 3/61 catheters collected, of which only two were blocked by mineral encrustations. In total, five catheters were blocked and *E. coli* and *E. faecalis* were the most common organisms isolated from the blocked catheter lumens, which is interesting as neither produces urease, which is cited as the cause of catheter blockage(10).

60.7% of lumens and 57.4% of balloons were colonised by two or more organisms. This proportion is slightly lower than that found by Warren et al, who reported that 77% of their catheter urine specimens were polymicrobial, though they did not examine the catheters(11). 34.4% of the bladder contents as represented by the balloon isolates were different from those in the lumen. Additional organisms may be detected in catheter urine culture as these can be released into the passing urine, and culture results may adversely influence treatment. This can be seen from the lack of correlation between the catheter contents and the CSU results. This is in agreement with a study by Montgomerie et al who investigated the colonisation of the urethral meatus and urine cultures in those that perform intermittent catheterisation, and found that there was no correlation between urethral colonisation and urine samples (12). Quite often the lack of consistency comes from an additional organism not being recorded. For example, one catheter grew 10^7 and 10^6 CFU/mL *E. coli* and E. *faecalis* respectively from the catheter lumen and balloon, whereas only *E. coli* was recorded in the CSU report despite both present in large quantities. The patient was treated with iv piperacillin-tazobactam when both isolates were sensitive to nitrofurantoin. Therefore, the

usefulness of CSUs is debatable given that they do not necessarily represent the microenvironment in the catheter lumen and more importantly, the catheter balloon, and do not appear to guide antibiotic prescribing. This then revisits the importance of symptom presentation as being the guiding factor for diagnosis and treatment of CAUTI.

These data, which show no effect of antibiotics on the reduction of attached bacteria in the catheter, support the Scottish Intercollegiate Guidelines Network (13) and the Infectious Disease Society of America (14) recommendations for changing the catheter before starting antibiotic treatment for CAUTI. Antibiotics do not reduce attached biofilm bacteria and are likely to be a driver of antibiotic resistance. The higher proportion in this study of MDR isolates from catheters of patients receiving antibiotics may due to the influence of antibiotics, or it may be that MDR organisms more often cause symptoms and therefore require antibiotic treatment.

The relationship between the time the catheter remains in situ and increased rate of bacteriuria, incurring an increased risk of 5% per day, is well-established in the literature (15). From 10 days onwards, 96.7% of the catheter lumens and balloons were colonised in our study. There was no evidence of the number or quantity of species increasing from 10 days to 119 days, which was the longest duration of catheterisation in this study. It appears that by day 10, colonisation of the catheter may be established and thus there may not be capacity within the catheter to support additional microorganisms. In a study by Ganderton et al (16), there was no relationship between duration of catheterisation and amount of biofilm. In our study, there was also no difference between the number of species or the quantity of each isolate in those patients who were symptomatic and those who were asymptomatic. This again reinforces the emphasis for diagnosis to be placed on symptom presentation and not solely on the microbiological results, which may not accurately reflect the bladder contents as seen from the CSU results.

Author Contributions:

KB(https://orcid.org/0000-0001-5893-0882): conceptualisation, methodology, investigation, writing- original draft, writing – review and editing

SK: Investigation, writing – review and editing

KA: Investigation, writing – review and editing

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Figure legends:

Figure 1: Correlation of A.) The number of isolates in each catheter lumen and B.) the quantity (CFU/mL) of each isolate in each catheter plotted against length of time the catheter was in situ. The Pearson correlation coefficient was computed and indicated no correlation of variables.

Tables:

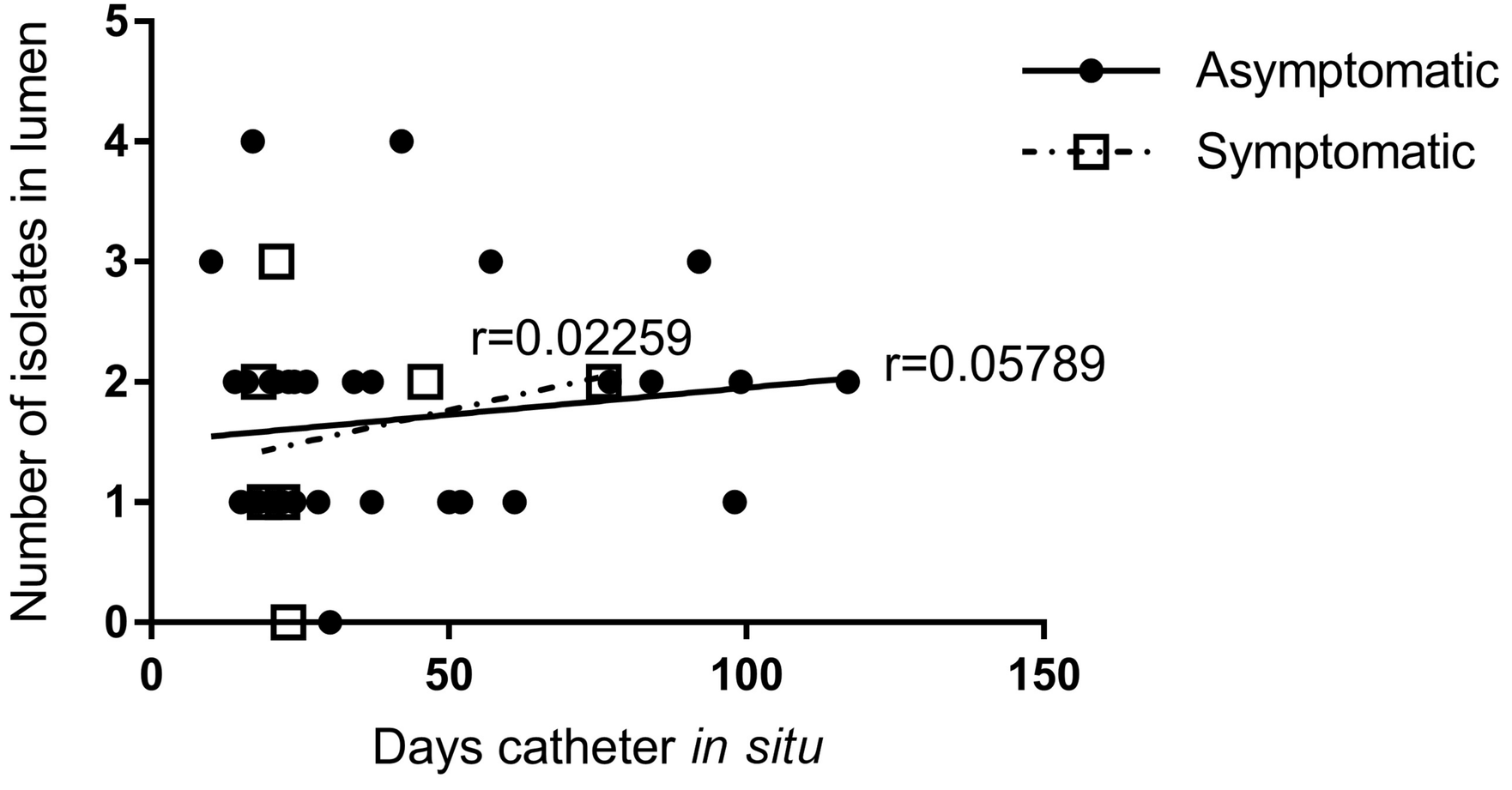
Table I: Inventory of microorganisms isolated from the balloons and lumens of indwelling urethral urinary catheters in situ for 10 days or greater.

Organisms isolated from catheter lumens			**Organisms isolated from catheter balloons**	
Enterobacteriaceae	**47**		**Enterobacteriaceae**	**40**
Escherichia coli	24		*E. coli*	20
Klebsiella pneumoniae	5		*Klebsiella pneumoniae*	5
Enterobacter cloacae	4		*Enterobacter cloacae*	4
Klebsiella oxytoca	3		*Klebsiella oxytoca*	3
Proteus mirabilis	3		*Morganella morganii*	2
Morganella morganii	2		*Citrobacter koseri*	1
Serratia liquefaciens	2		*Citrobacter koseri/amalonaticus*	1
Hafnia alvei	1		*Hafnia alvei*	1
Pantoea spp.	1		*Pantoea* spp.	1
Citrobacter koseri	1		*Proteus mirabilis*	1
Citrobacter koseri/amalonaticus	1		*Serratia liquefaciens*	1
Enterococci	**18**		**Enterococci**	**20**
Enterococcus faecalis	17		*Enterococcus faecalis*	19
Enterococcus faecium	1		*Enterococcus faecium*	1
Pseudomonas spp.	**16**		**Pseudomonas spp.**	**12**
Staphylococci	**14**		**Staphylococci**	**19**
Staphylococcus epidermidis	4		*Staphylococcus epidermidis*	9
Staphylococcus aureus	3		*Staphylococcus aureus*	3
Staphylococcus capitis	2		*Staphylococcus caprae*	2
Staphylococcus haemolyticus	2		*Staphylococcus haemolyticus*	2
Staphylococcus caprae	1		*Staphylococcus xylosus*	1
Staphylococcus lugdunensis	1		*Staphylococcus hominis*	1
Staphylococcus saprophyticus	1		*Staphylococcus saprophyticus*	1
Staphylococcus xylosus	1			

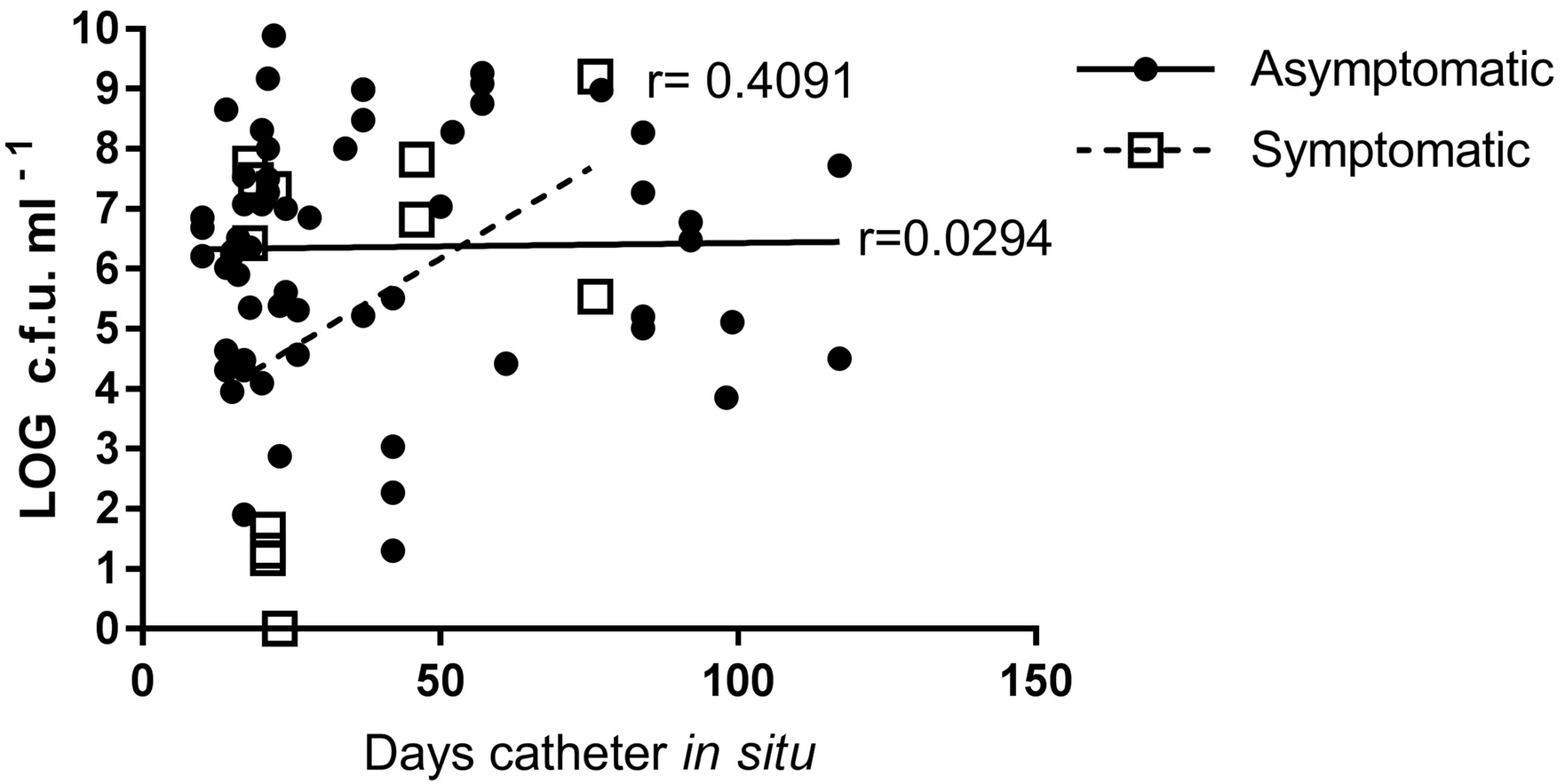
			Yeasts	**7**
Yeasts	**6**		*Candida albicans*	4
Candida albicans	4		*Candida glabrata*	1
Candida guilliermondii	1		*Candida guilliermondii*	1
Candida parapsilosis	1		*Candida parapsilosis*	1
Others	**6**		**Others**	**5**
Micrococcus spp.	2		*Streptococcus agalactiae*	1
Corynebacterium propinquum	1		*Streptococcus bovis*	1
Streptococcus agalactiae	1		*Streptococcus gordonii*	1
Streptococcus bovis	1		*Streptococcus intermedius*	1
Streptococcus intermedius	1		*Corynebacterium propinquum*	1
Total:	**107**		**Total:**	**103**

337

a.)


Number of isolates in lumen
0
1
2
3
4
5
0
50
100
150
Days catheter *in situ*
r=0.02259
r=0.05789
Asymptomatic
Symptomatic

b.)


LOG c.f.u. ml -1
0
1
2
3
4
5
6
7
8
9
10
0
50
100
150
Days catheter *in situ*
r= 0.4091
r=0.0294
Asymptomatic
Symptomatic