Role of asymptomatic bacteriuria on early periprosthetic joint infection after Hip Hemiarthroplasty. BARIFER randomized clinical trial.

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Abstract

Purpose: To evaluate preoperative asymptomatic bacteriuria (ASB) treatment on the reduction of early-periprosthetic joint infections (early-PJIs) after hip hemiarthroplasty (HHA) for fracture.

Methods: Open-label, multicentre RCT comparing 3gr of fosfomycin-trometamol with non-treatment. A parallel follow-up cohort without ASB was established. Primary outcome: early-PJI within 3 months after HHA.

Results: 594 patients enrolled (mean age 84.3years); 152(25%) with ASB (77 treated with fosfomycin and 75 controls) and 442(75%) without. ASB was not a predictor of early-PJI (OR:1.06[95%CI:0.33-3.38], *p*=0,9228) and its treatment did not modify early-PJI incidence (OR:1.03[95%CI:0.15-7.10], *p*=0.9787).

Conclusions: Neither preoperative ASB nor its treatment were risk factors of early-PJI after HHA.

Trial Registration: Eudra CT 2016-001108-47

Introduction

Early-periprosthetic joint infection (early-PJI) after joint replacement is a challenging complication. Rates of early-PJI are higher in HHA patients than in total hip arthroplasty (THA) and range between 1.3–9%[1–5].

Bacterial colonization of the genitourinary tract as an infection cause of hip prostheses during a haematogenous seeding or due to contamination of the skin by continuity has been suggested. This asymptomatic colonization is called asymptomatic bacteriuria (ASB) and its prevalence reaches 30–50% in elderly women in long-term care facilities [6]. Published studies demonstrated that preoperative ASB treatment among candidates for elective total hip and knee arthroplasties has no impact in early-PJI [7–11]. However, its impact on patients undergoing HHA is a matter of controversy with a single-center study concluding that treating ASB in geriatric patients with a femur fracture decreases the risk of PJIs [12].

We evaluate the impact of preoperative ASB treatment in the cumulative incidence of early-PJI in patients undergoing HHA for a hip fracture. We hypothesized that preoperative ASB treatment in these patients could decrease the incidence of early-PJI caused by Gram-negative bacilli (GNB).

Patients And Methods

BARIFER was a phase IV, multicentre, randomized, open-label and parallel-group clinical trial conducted at 11 sites in Spain designed to evaluate the impact of treating ASB on the incidence of early-PJI in HHA.

All patients provided informed consent. Protocol approval was obtained from an independent ethics committee at each site. The trial (EudraCT 2016-001108-47) was performed under the principles of the

Declaration of Helsinki. Adherence to the Consolidated Standards of Reporting Trials [13] (CONSORT) is supported by the completed checklist provided as Supplementary material.

Patients ≥18 years requiring HHA for fracture were recruited. Exclusion criteria include any concomitant infection requiring antibiotics and hip fractures treated with screws or THA.

Urine analysis was performed before HHA surgery. ASB referred to a urine culture growing $\geq 10^5$ colony-forming units/mL of a bacterial species in a patient lacking symptoms of a urinary tract infection (UTI). All microorganisms isolated were identified by standard procedures. Antimicrobial susceptibility was performed by microdilution (Vitek bioMérieux, France). The MIC values of fosfomycin were interpreted according to EUCAST criteria 2012 (version 2.0) guidelines (www.eucast.org).

Participants with ASB were randomly assigned in a 1:1 ratio, centralized and stratified by centre, to receive 3 g of fosfomycin-trometamol (oral route) *vs.* no treatment, between 24 and 6h before surgery. A parallel follow-up cohort of HHA candidates without ASB was established.

Preoperative antibiotic prophylaxis was decided according to each centre protocol (Supplementary Table 1). All patients were followed for 3 months after HHA or until early-PJIs or death was diagnosed, whichever occurred first.

PJIs occurring within 3 months after HHA were considered early-PJIs [14]. Patients were diagnosed with a PJI following diagnostic criteria established by the Infectious Diseases Society of America [15]. In case of early-PJI, a new visit was completed in which the microorganism causing the infection was recorded.

Primary outcome: cumulative incidence of early-PJI after preoperative ASB treatment. Secondary analyses included global incidence of ASB and early-PJI, risk factors for early-PJI and safety of fosfomycin treatment.

Statistical Analysis

Categorical variables were presented as number and percentages and quantitative variables as a median and interquartile range or a mean and standard deviation, as appropriate. Comparative analyses were performed using X^2 or Fisher's test for categorical variables, and Student's t-test or Mann–Whitney U-test for continuous variables. Level of significance was set to $p < 0.05$. Predictors of early-PJI were determined by univariate analysis. The Kaplan-Meier method was used to describe cumulative probability early-PJI stratified by study group.

The EAST program calculated the sample size. We assumed a prevalence of ASB up to 20% in men and 50% in women, an incidence of 9% of early-PJI and an expected 50% reduction with fosfomycin treatment with a test power of 90% and alpha error of 0.05. We needed 1394 patients (697 in each treatment group). An interim analysis was planned to stop the study in case it would not be possible to test the hypothesis. Analyses were performed with STATA 15.1 software (StataCorp, TX, USA) in the intention-to-treat (ITT) population.

Results

A total of 594 patients were included from September 2016 to November 2018. Overall, 420(71.0%) were women and the mean age was 84.3 years. ASB was diagnosed in 152(25%) patients, 77 treated with Fosfomycin and 75 untreated controls. Figure 1 shows the flow chart of patients' distribution.

Patients with ASB versus the non-ASB group were mostly women, with a higher Charlson comorbidity index score and more commonly with urinary incontinence (Table 1). Supplementary table 2 shows causative isolates of ASB. As expected, 82% were GNBs (Mostly *Escherichia coli* and *Klebsiella* spp.) of which 89% were susceptible to fosfomycin. Table 2 compares baseline characteristics of treated and untreated patients with ASB.

HHA implants were 65.46% cemented with antibiotics (64% with single-antibiotic and 36% with dual-antibiotic Vancogenx®).

Overall, 558(93.9%) patients (140 with ASB and 418 without) completed 3 months of follow-up (Table 3). Early-PJI rate was 2.5% (15 of 594 patients). Of these 15 patients, 4(2.7%) showed previous ASB but only 2 were treated with fosfomycin (Table 3). Our trial showed that treating preoperative ASB does not modify the incidence of early-PJI (OR: 1.03 [95%CI: 0.15-7.10], p= 0.9787). Of note, all early-PJI occurred within 60 days after HHA (Figure 2). Table 4 shows the aetiology of the 15 early-PJIs. We observed a lack of correspondence between ASB and early-PJI causing microorganisms. Univariate analysis of risk factors for early-PJI is presented in Table 5. Preoperative ASB was not a predictor of early-PJI (OR: 1.06 [95%CI: 0.33-3.38], p= 0.9228).

AEs related to Fosfomycin occurred in 4 patients, all of them of mild intensity. Three patients suffered from nausea and one reported dizziness (Supplementary Table 3).

Discussion

Identifying potentially modifiable preoperative risk factors of PJIs is of great interest. Experts traditionally recommended treating ASB before THA [16–19] although the latest published studies contradict this recommendation [7,8,10,11]. There are only two previous randomized controlled trials addressing this subject including both THA and HHA [7,8]. Our findings suggest that preoperative ASB treatment does not have an impact on the reduction of early-PJI after HHA. Ours is the first randomized trial which only enrolled this subgroup of patients.

The prevalence of ASB in our cohort was 25% which is higher than in THA candidates [7,8,16] and consistent with data reported for HHA [20]. Female sex, adjusted Charlson index and urinary incontinence are significantly more prevalent in the ASB group as previously reported [7].

Almost 90% of the identified GNB causing ASB were susceptible to fosfomycin as previously published [21,22]. The efficacy of a single dose of fosfomycin-trometamol for uncomplicated lower UTI is

comparable with standard regimens with fluoroquinolones or trimethoprim/sulfamethoxazole [23] and easier to administer, therefore, it was chosen as preoperative treatment. Fosfomycin has a low incidence of AEs which mainly comprise mild and transient gastrointestinal symptoms [23]. This matches our study as only 4 patients experienced some associated nausea or dizziness.

Only 4 patients with ASB had an early-PJI which represents an incidence of 2.7%. Although this is lower than expected [4,7,8], it is consistent with the latest data collected in the VINCat registry (surveillance database of nosocomial infections in Catalonia) [5]. When investigating risk factors for early-PJI our study focuses on preoperative ASB. In our series ASB is not a risk factor for early-PJI unlike other published data showing that, although the risk of PJI is not influenced by ASB treatment, there seems to be an increased risk of PJI in this population [7]. It is also remarkable that in no case the microorganism causing ASB was identical as the one causing early-PJI which has also been highlighted by other authors [7,24]. In our experience ASB treatment does not modify the incidence of early-PJI. Although we observed a delay from HHA surgery to onset of infection of about 10 days higher in patients treated with Fosfomycin, the exceptionally low number of events prevents us from reaching any conclusion. Therefore, since we have not been able to demonstrate a potential benefit in treating preoperative ASB we do not recommend systematic urinalysis screening and treatment.

Also noteworthy is the percentage of antibiotic-loaded cement used. Published studies show that it leads to a reduction in the rate of PJIs in HHA with no associated increase in complications [25–27]. This approach could justify a global reduction of early-PJ rates compared to our previous incidence between 2011 and 2013 [4].

Finally, global mortality in our series is high (9% of our patients) but it could be explained by the age and comorbidity of the population, particularly among those with ASB, as evidenced by the high Charlson comorbidity index values [1,28].

The main limitation of our study is the small sample size. The difficulty of obtaining informed consent signature in time to complete the entire inclusion process at least 6 hours before surgery made our inclusion rate slow. We did an interim analysis that showed that it would not be possible to test the hypothesis and for this reason we decided to end the study. It is also possible that we overestimate the incidence of early-PJI after HHA and therefore the study might be underpowered to confirm the hypothesis. The main strengths of the study are its design (randomized trial) and having included geriatric patients (frequently underrepresented in clinical trials) all of them undergoing HHA.

In conclusion, our results suggest that ASB is not an independent risk factor for early-PJ and its treatment did not reduce the incidence of early-PJI after HHA. Therefore, we cannot recommend routine screening and treatment of preoperative ASB in HHA surgery.

Part of this study was presented at the XXIII Congreso Nacional de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica, which took place in Madrid, on 23-25th May 2019.

Declarations

Supplementary Data

Supplementary materials are available online.

Notes

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Transparency declaration

The authors declare that they have no conflict of interest.

Author's contributions

Dr Rodriguez-Pardo and Dr Pigrau contributed to its Conception, Clinical trial design, Protocol, Data collection, Patient recruitment, Data analysis and writing the paper with the assistance of a medical writer. Dr Corona and Dr Almirante contributed to its Conception, Clinical trial design and Reviewing and editing the manuscript. All the other authors participated in Patient recruitment, Data collection, Reviewing and editing the manuscript. All authors approved the submitted versions, had full access to the data (under confidentiality agreements), and vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol.

LIST OF COLLABORATORS/GROUP OF INVESTIGATORS FOR BARIFER CLINICAL TRIAL

This is a multicentre study. In each institution there are many researchers that have helped to make this study possible. We are deeply indebted to these collaborators, who are:

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Tables

Table 1. Baseline demographics and clinical characteristics of patients (ITT analysis)

Characteristics	Patients with ASB (n = 152, 100%)	Patients without ASB (n = 442, 100%)	Total (n = 594,100 %)	P Value	OR (95% CI)
Age, mean (SD)	84.5 (7.9)	84.2 (8.5)	84.3 (8.34)	0.7725	1.003 (0.981; 1.026)
Median (Q1-Q3), y	86.0 (81.7; 89.6)	86.0 (80.6;89.7)	86.0 (80.7; 89.7)		
Female sex	124 (81.6%)	296 (67.0%)	420 (70.7%)	0.0008	2.18 (1.39; 3.44)
Comorbid conditions					
BMI mean (SD)	24.4 (4.5)	24.3 (3.5)	24.4 (3.8)	0.8319	1.01 (0.95; 1.07)
Median (Q1-Q3), kg/m2	24.8 (21.5;26.6)	24.2 (21.6;26.6)	24.2 (21.6;26.6)		
Obesity (BMI ≥ 30 kg/m2)	9 (8.3%)	14 (5.3%)	23 (6.2%)	0.2886	1.46 (0.73; 2.95)
Cardiac failure	19 (12.6%)	45 (10.2%)	64 (10.8%)	0.4124	1.27 (0.72; 2.25)
Peripheral vasculopathy	15 (9.9%)	41 (9.3%)	56 (9.4%)	0.8114	1.27 (0.58; 2.01)
Diabetes	45 (29.8%)	106 (24.0%)	151 (25.4%)	0.1573	1.35 (0.89; 2.03)
Dementia	50 (33.1%)	118 (26.7%)	168 (28.3%)	0.1317	1.36 (0.91; 2.03)
Chronic bronchopathy	19 (12.6%)	49 (11.1%)	68 (11.5%)	0.6184	1.15 (0.66; 2.03)
Cirrhosis	6 (3.97%)	6 (1.4%)	12 (2.0%)	0.0600	3.01 (0.95; 9.47)
Chronic renal failure	28 (18.4%)	67 (15.1%)	95 (16.0%)	0.3446	1.26 (0.78; 2.05)
Charlson index score*					
mean (SD)	6.1 (2.2)	5.6 (1.9)	5.8 (2.0)	0.0146	1.12 (1.02; 1.22)
median (Q1-Q3)	6.0 (5.0; 7.0	5.0 (4.0; 7.0)	6.0 (4.0; 7.0)		
Urinary incontinence	52 (34.4%)	78 (17.7%)	130 (22.0%)	<0.0001	2.44 (1.61; 3.70)
Rheumatoid arthritis	1 (0.7%)	8 (1.8%)	9 (1.5%)	0.3395	0.36 (0,04;2.92)
Immunosuppressors**	7 (4.6%)	25 (5.6%)	32 (5.4%)	0.6121	0.81

					(0.34;1.90)
Malignancy	11 (7.2%)	32 (7.2%)	43 (7.2%)	0.9990	1.00 (0.491; 2.04)
Anticoagulant treatment	40 (26.5%)	101 (22.8%)	141 (23.8%)	0.3649	1.22 (0.80; 1.86)
Antiplatelet treatment	44 (29.1%)	130 (29.4%)	174 (29.3%)	0.9493	0.36 (0.04; 2.92)

Unless otherwise specified, data represent No. (%) of patients.

Abbreviations: ITT, intention to treat analysis; ASB, asymptomatic bacteriuria; OR, odds ratio; CI, confidence interval; SD, Standard Deviation; BMI, body mass index

*Charlson index score is adjusted by age

** Immunosuppressors includes steroids, classic immunosuppressors (ie: methotrexate, azathioprine, mycophenolate), biological drugs and chemotherapy

Table 2. Baseline characteristics of Treated and Untreated Patients with ASB.

	Patients, No. (%)		
Characteristic	Untreated ASB (N= 75, 100%)	ASB treated with Fosfomycin (N=77, 100%)	Total (N=152, 100%)
Age, mean (SD), y	84.2 (8.6)	84.6 (7.2)	84.5 (7.9)
Median (Q1-Q3), y	85.9 (81.6;89.9)	86.15 (81.7;89.4)	85.96 (81.7;89.6)
Female sex	59 (78.7%)	65 (84.4%)	124 (81.6%)
Comorbid conditions			
BMI[a] mean (SD), y	24.6 (4.7)	24.2 (4.1)	24.4 (4.46)
Median (Q1-Q3), y	24.9 (21.6;26.7)	23.5 (21.5;26.6)	24.8 (21.5;26.6)
Cardiac failure	11 (14.9%)	8 (10.4%)	19 (12.6%)
Peripheral vasculopathy	8 (10.8%)	7 (9.1%)	15 (9.9%)
Cerebral vasculopathy	14 (18.9%)	13 (16.9%)	27 (17.9%)
Dementia	22 (29.7%)	28 (36.4%)	50 (33.1%)
Chronic Bronchopathy	12 (16.2%)	7 (9.1%)	19 (12.6%)
Cirrhosis	3 (4.0%)	3 (3.1%)	6 (4.0%)
Diabetes	24 (32.4%)	21 (27.3%)	45 (29.8%)
Chronic renal failure	14 (18.7%)	14 (18.2%)	28 (18.4%)
Malignancy	6 (8.7%)	5 (6.5%)	11 (7.3%)
Immunosuppressors**	7 (9.3%)	1 (1.3%)	8 (5.3%)
Anticoagulant treatment	20 (27.0%)	20 (26.0%)	40 (26.5%)
Antiplatelet treatment	23 (31.1%)	21 (27.3%)	44 (29.1%)
Rheumatoid arthritis	1 (1.3%)	0 (0%)	1 (0.7%)
Urinary incontinence	27 (36.5%)	25(32.5%)	52 (34.4%)
Charlson index score*			
mean (SD)	6.19 (2.3)	6.0 (2.2)	6.1 (2.2)
median (Q1-Q3)	6.0 (5.0;8.0)	6.0 (4.0;7.0)	6.0 (5.0;7.0)
Days from admission to HHA*			
mean (SD)	4.3 (6.9)	3.7 (2.2)	4.0 (5.1)

median (Q1-Q3)	3.0 (2.0;5.0)	3.0 (2.0;5.0)	3.0 (2.0;5.0)
Duration of HHA surgery			
mean (SD), min	94.9 (27.2)	93.26 (23.4)	94.1 (25.4)
median (Q1-Q3), min	90.0 (75.0;120.0)	90.0 (80.0;5.0)	90.0 (75.0;115.0)
Duration of HHA surgery > 75th percentile	17 (28.3%)	12 (21.0%)	29 (24.8%)
Antibiotic Cemented HHA	67 (89.3%)	66 (89.2%)	133 (89.3%)
HHA dislocation	4 (5.3%)	4 (5.2%)	8 5 (26%)
Postoperative UTI	6 (8%)	7 (9.1%)	13 (8.5%)
Postoperative infection other than UTI	4 (5.3%)	3 (3.9%)	7 (4.6%)
Patients transferred to a convalescence centre	28 (40%)	35 (50%)	53 (37.9%)

Unless otherwise specified, data represent No. (%) of patients.

Abbreviations: ASB, asymptomatic bacteriuria; BMI, body mass index; ASA, American society of anesthesiologists; HHA, hip hemiarthroplasty; UTI, urinary tract infection; PJI, periprosthetic joint infection.

[a] Data available for 109 patients (58 untreated ASB and 51 treated ASB)

* Charlson index score is adjusted by age.

** Immunosuppressors includes steroids, classic immunosuppressors (ie: methotrexate, azathioprine, mycophenolate), biological drugs and chemotherapy

Table 3. Overall outcomes (ITT analysis)

Outcome	ASB Patients		Non-ASB Patients	Total
	Not treated with Fosfomycin	Treated with Fosfomycin		
	75 (100%)	77 (100%)	**442 (100%)**	**594 (100%)**
No HHA infection after 12 weeks	59 (78.7%)	56 (72.7%)	369 (83.5%)	484 (81.7%)
Death within 12 weeks	9 (12%)	11 (14.3%)	34 (7.7%)	54 (9%)
Early-PJI	2 (2.7%)	2 (2.6%)	11 (2.5%)	15 (2.5%)
Loss of follow-up	4 (5.3%)	8 (10.4%)	25 (5.6%)	36 (6.1)
Prostheses removed due to orthopaedic reasons	1 (1.3%)	0 (0%)	3 (0.7%)	4 (0.7%)

Abbreviations: ITT, Intention to treat; ASB, Asymptomatic bacteriuria; HHA, Hip hemiarthroplasty; PJI, periprosthetic joint infection

Table 4. Aetiology, relationship with ASB and outcome of early-PJI infections

Patients	Patients without ASB	Patients with ASB		Aetiology of early-PJI	Aetiology of ASB
		Treated with Fosfomycin	Not treated with Fosfomycin		
1	x			MSSA	
2		x		*S. epidermidis*	*E. coli*
3	x			*MSSA*	
4			x	*C. striatum*	*K. pneumoniae*
5	x			*E. coli* ESBL *producer*	
6	x			*E. coli ESBL producer*	
7	x			*MRSA.*	
8	x			*K. pneumoniae*	
9		x		*MRSA*	*E. coli ESBL producer*
10	x			*E. coli ESBL producer**	
11	x			*S. epidermidis*	
12			x	*S. epidermidis* *Bacillus* spp. *S. haemolyticus*	*E. coli*
13	x			Negative culture≠	
14	X			Negative culture≠	
15	x			*E. faecalis*	

Abbreviations: HHA, Hip Hemiarthroplasty; ASB, asymptomatic bacteriuria; PJI, prosthetic joint infection; MSSA, methicillin susceptible *S. aureus*; MRSA, methicillin resistant *S. aureus*; *ESBL* producer, extended spectrum beta-lactamase producer

* This patient was diagnosed with a postoperative UTI caused by *E. coli ESBL* producer.

≠Although purulence was observed at surgical debridement in those 2 cases, both under broad-spectrum antibiotic treatment at that time, cultures were negative.

Table 5. Univariate analysis of risk factors for early-PJI (ITT analysis)

Risk factor	Patients, No. (%) N=594		Univariable Analysis	
	No HHA infection N= 579, 100%	HHA infection N =15, 100%	P value	OR (95%CI)
Age, mean (SD), y	84.3 (8.4)	85.1 (5.0)	0.7163	1.01 (0.95;1:08)
Age, median (Q1-Q3), y	85.96 (80.7;89.7)	86.0 (81.1;88.9		
Female sex	409 (70.6%)	11 (73.3%)	0.8210	1.14 (0.36;3.64)
Comorbid conditions				
Preoperative ASB	148 (25.6%)	4 (26.7%)	0.9228	1.06 (0.33;3.38)
BMI mean (SD)	24.3 (3.8)	25.6 (2.5)	0.2712	
Median (Q1-Q3), kg/m2	24.2 (21.7;26.5)	25.9 (22.9;27.3)		
Obesity (BMI ≥ 30 kg/m2)	22 (6.1%)	1 (9.1%)	0.5103	1.00 (1.00;1.00)
Ischemic heart disease	48 (8.3%)	1 (6.7%)	0.8205	0.79 (0.10;6.13)
Dementia	161 (27.1%)	7 (46.7%)	0.1197	2.27 (0.81; 6.35)
Cirrhosis	11 (1.9%)	1 (6.7%)	0.2270	3.68 (0.44;30.51)
Diabetes	147 (25.4%)	4 (26.7%)	0.9138	1.07 (0.33;3:40)
Charlson index score*				
mean (SD)	5.7 (2.0)	6.4 (2.9)	0.2198	1.15 (0.92;1.44)
median (Q1-Q3)	6.00 (4,0; 7.0)	6.0 (4.0; 7.0)		
Immunosuppressors**	32 /5.5%)	0 (0%)	0.3492	1.00 (1.00; 1.00)
Malignancy	40 (6.9%)	3 (20%)	0.0682	3.37 (0.91;12.43)
Anticoagulant treatment	136 (23.5 %)	5 (33.3%)	0.3659	1.63 (0.55;4.84)
Antiplatelet treatment	171 (29.5%)	3 (20%)	0.4258	0.60

				(0.17;2.14)
Days since admission to HHA				
mean (SD)	4.26 (4.8)	4.7 (2.9)	0.7412	1.01 (0.93;1.10)
median (Q1-Q3)	3.00 (2.0; 5.0)	4.00 (3.0; 6.0)		
Days since admission to HHA > 75th percentile	113 (19.5%)	5 (33.3%)	0.1957	2.06 (0.69;6.14)
Duration of HHA surgery				
mean (SD), min	93.97 (25.57)	100.0 (17.3)	0.6863	1.01 (0.96;1.06)
median (Q1-Q3), min	90 (75.0; 115.0)	90 (90.0; 120.0)		
Duration of HHA surgery > 75th percentile	28 (24.6%)	1 (33.3%)	0.7302	1.54 (0.13;17.58)
Antibiotic Cemented HHA	372 /568 (65.6%)	9 /15 (60%)	0.7351	0.83 (0.29;2.38)
HHA dislocation	13 (2.2%)	1 (6.7%)	0.2901	3.11 (0.38;25.45)
Any postoperative infection	36 (6.2%)	4 (26.7%)	0.0052	5.48 (1.66;18.08)

Unless otherwise specified, data represent No. (%) of patients.

Abbreviations: PJI, prosthetic joint infection; ITT, intention to treat analysis; HHA, hip hemiarthroplasty; BMI, body mass index; ASB, asymptomatic bacteriuria; OR, odds ratio; CI, confidence interval; SD, standard deviation.

* Charlson index score is adjusted by age

** Immunosuppressors includes steroids, classic immunosuppressors (ie: methotrexate, azathioprine, mycophenolate), biological drugs and chemotherapy

N/N with data available when appropriate

Figures

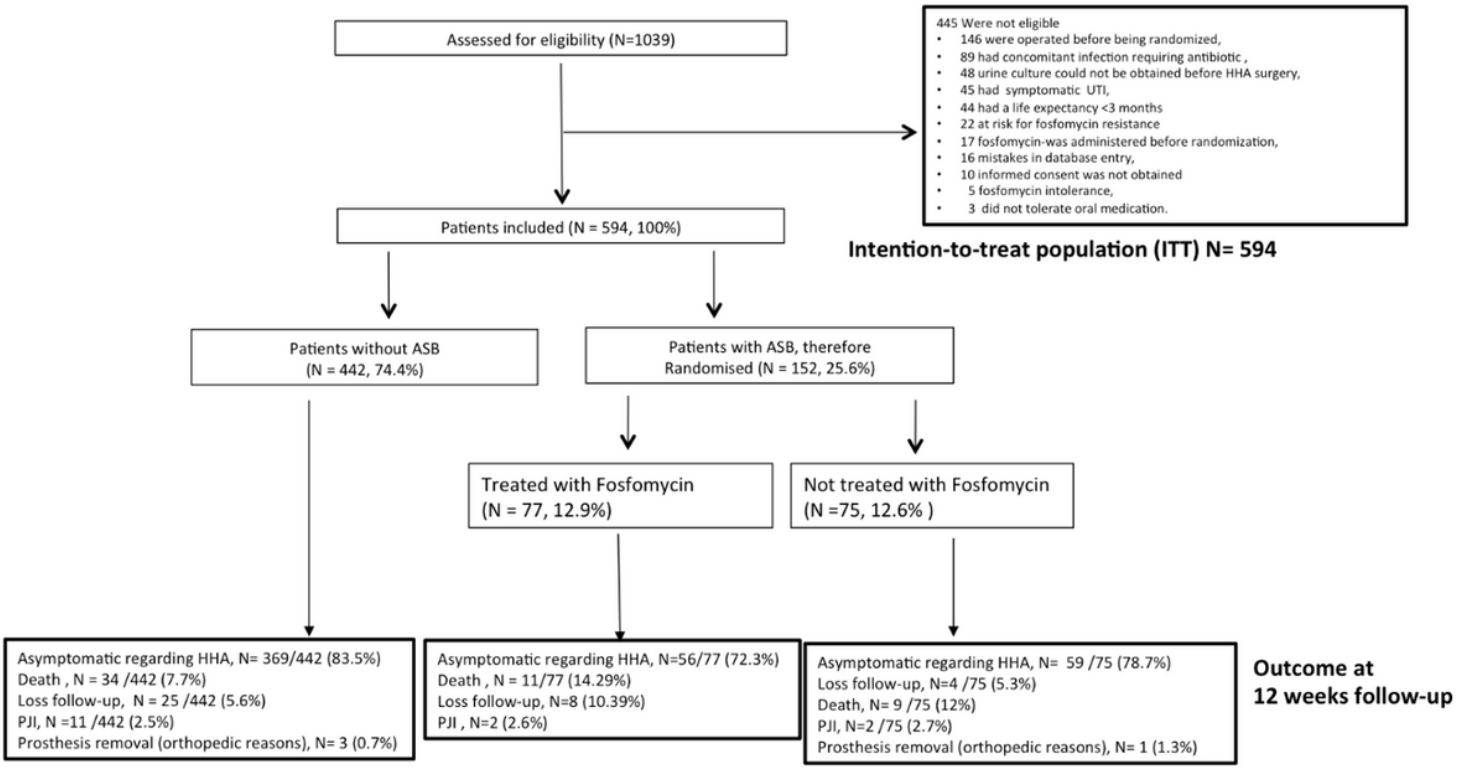

Figure 1

Overall flow chart and outcome of patients included in BARIFER clinical trial (ITT analyses), N= 594. Abbreviations: ITT, intention to treat; UTI, urinary tract infection; ASB, asymptomatic bacteriuria; PJI, periprosthetic joint infection. 22 patients with ASB were considered at risk for Fosfomycin resistance as they were under chronic antibiotic prophylaxis with Fosfomycin-trometamol for recurrent cystitis. Therefore, they were not randomized.

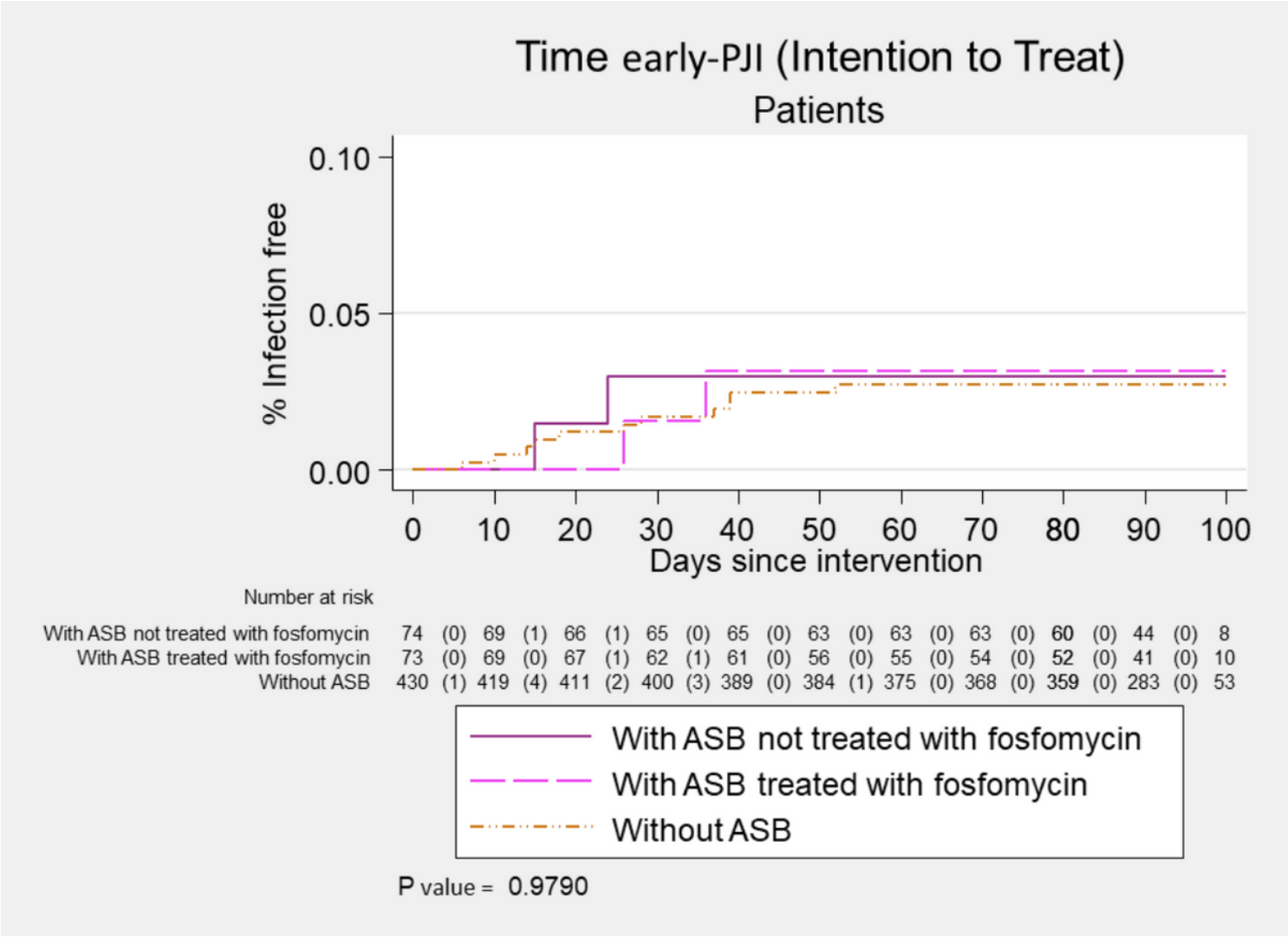

Figure 2

Distribution of the time to early-PJI according to study group. Abbreviations: Early Periprosthetic Joint Infection

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- BriefreportBARIFERSupTable1EJCMID.docx
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