



Original article

Obesity and smoking predict the results of two-stage exchange in septic revision hip arthroplasty: A cohort study

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ABSTRACT

Background: Prosthetic joint infection (PJI) is deemed to be the most serious complication following total hip arthroplasty. Obesity and smoking are known risk factors for PJI. However, the influence of these variables on infection free survival, of septic revision hip arthroplasty, is yet to be explored. The aim of this study was to determine the effect of obesity and smoking on the outcome of two-stage prosthetic exchange surgery.

Patients and methods: A consecutive series of 97 hips in 94 patients (69 male, 25 female, mean age 66 ± 12 years), undergoing two-stage revision surgery for hip PJI, were investigated retrospectively, after a mean follow-up of 60 (24–170) months. Survival was estimated using Kaplan-Meier curves. A multivariate cox-regression model was applied to test for the influence of smoking or obesity ($BMI \geq 30$) after adjusting 16 potential patient-dependant variables.

Hypothesis: The study hypothesis was that smoking and high BMI are predictors for the failure of septic revision hip arthroplasty. Failure of septic revision hip arthroplasty was defined as failure to eradicate the infection or eradication of the infection but failure to preserve the arthroplasty.

Results: Kaplan-Meier showed a cumulative survival proportion of 80.4% (standard error S.E 4%), of the definitive implant, at 5 years. Obese patients ($BMI \geq 30$) and smokers had a significantly lower 5-year survival of 60.9% (S.E 1%) and 50.6% (S.E 1.4%), respectively ($p = 0.001$).

Discussion: Obesity and smoking are both factors determining infection free survival in two-stage revision hip arthroplasty. Clinicians should be aware of potential complications and anticipate a higher likelihood of conversion to a Girdlestone resection or even amputation in this group of patients.

Level of evidence: III, retrospective cohort study.

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1. Introduction

The orthopaedic community is increasingly encountering complications of primary joint replacement. The need for evidence-based algorithms to optimize complication management became ultimately clear, resulting in an increased research output throughout the recent years.

Prosthetic joint infection (PJI) is regarded to be the most severe complication following total hip arthroplasty. Studies have reported a peak incidence of 2.2% for primary hip arthroplasty [1]. Furthermore, PJI can not only impose a huge economic burden, but the associated psychological and physical stress may damage the

patient-physician trust. Therefore, a well-judged management plan is critical when treating post-surgical PJI [2].

Several treatment options for PJI have been reported throughout the recent years. Treatments include debridement and retention, single-stage revision, resection arthroplasty, long-term antibiotic suppression and two-stage revision [3–6]. The latter being considered the gold standard for eradicating PJI, with success rates reported as being as high as 94% [7,8].

Obesity is a well-established risk factor for osteoarthritis. Furthermore, patients undergoing revision arthroplasty are generally more likely to be obese [9,10]. The risk of prosthetic joint infection was found to be notably higher amongst patients who smoke and patients with a BMI of higher than 40 kg/m^2 [11,12]. However, a positive effect of weight loss prior to arthroplasty surgery has not yet been established, since some reports suggest possible adverse effects of weight loss prior primary arthroplasty surgery [13,14].

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Despite the fact that morbid obesity and smoking are known to be risk factors for prosthetic joint infection, little is known about the effect these variables have on the revision surgery itself. Recent reports pointed towards obesity being a risk factor for failure of revision arthroplasty [15]. The primary aim of this study was to determine the influence of obesity and smoking on infection-free survival after two-stage revision hip arthroplasty. The second aim was to determine whether these factors influence the likelihood of conversion to a Girdlestone situation or the risk of amputation.

2. Patients and methods

2.1. Study design

Variables were retrieved retrospectively from patients, undergoing two-stage revision surgery for hip PJI, based on the following inclusion criteria:

- PJI diagnosis of a primary prosthetic joint;
- the interdisciplinary decision of a two-stage treatment strategy based on symptoms duration and soft tissue condition;
- a minimum follow-up of 24 months after implantation of the definitive revision hip arthroplasty, taking into account any failure event;
- all patients operated on by surgeons from the same department and with an experience in hip arthroplasty.

The study design constituted a regression model with patient-related factors as input variables and failure as an output endpoint, based on the definitions below.

2.2. Data acquisition and patient-dependent variables

The medical files of 94 patients fulfilling the inclusion criteria were retrieved and the following parameters were extracted: Age, gender, comorbidities such as diabetes, rheumatoid arthritis, immune suppression, psoriasis, corticosteroid use, rheumatoid arthritis (RA), gout, BMI, malignancies, smoking status, intravenous drug abuse, cardiac, liver or renal disease, alcoholism.

2.3. Treatment regime

All patients underwent a two-stage treatment protocol involving complete removal of the primary infected joint, with or without implantation of a gentamicin impregnated cement spacer as a first-stage procedure ($n=9$ [9%] temporary Girdlestone situation). All patients underwent 2 weeks of intravenous antibiotics followed by 10 weeks of oral antibiotics. After 2-week interval without antibiotic treatment, a diagnostic joint aspiration was performed. Upon negative microbiology, the second stage procedure was performed, which involved the removal of the cement spacer and the implantation of a revision implant. On the acetabular side, a Ganz reinforcement ring was used in all cases to reconstruct the socket. The reinforcement ring was used in conjunction with a cemented low profile polyethylene inlay (Zimmer Inc, Switzerland) or a cemented dual mobility inlay (Mathys Medical Inc., Switzerland). For femoral revision, a cementless modular revision stem (Revitan[®], Zimmer Inc. or Modular Revision Stem, Mathys Medical Inc., Switzerland) or a cemented standard stem (Exafit[®], Zimmer Inc, Switzerland or Centris[®], Mathys Medical Inc., Switzerland) was used. Microbiology samples were obtained with any re-implantation. Patients with persistent infection, underwent secondary surgery (debridement and implant retention, $n=2$, two-stage revision, $n=4$) or were treated with long-term suppression antibiotics ($n=5$). All patients received perioperative antibiotic

prophylaxis (2nd generation cephalosporin (cefuroxime) or 3rd generation cephalosporin (ceftriaxone) plus vancomycin).

2.4. End points

End points were defined as the failure to eradicate infection with isolation of a pathogen, after the definitive second step procedure. Functional failure was defined as the eradication of infection, with the conversion to a Girdlestone situation or amputation.

2.5. Synthesis of results and statistical analysis

Normally distributed data were presented as mean \pm standard deviation (SD). Survival was estimated using Kaplan-Meier and presented as the cumulative proportion of surviving a particular time point and standard error (S.E). Comparisons were performed using log rank test. Variables showing an influence on survival were adjusted using a multivariate cox-regression model. SPSS was used for statistical analysis (Version 24, IBM Inc., Armonk, NY).

The study was approved by the ethical committee of the Canton of Bern, Switzerland (Ref.-Nr. KEK-BE: 265/2014).

3. Results

3.1. Patient demographics

The cohort comprised 97 hips in 94 patients. The patients were diagnosed with PJI between 06/07/1999 and 01/10/2012. The mean follow up time was 60 months; range 24–170. There were 69 male and 25 female patients. Mean age was 66 ± 12 . Patient-related risk factors are illustrated in Table 1.

3.2. Treatment outcome

Eradication of the infection and successful re-implantation of a revision hip arthroplasty, i.e., without functional failure, was achieved in 67 hips. This was achieved with a two-stage revision in 61 out of these 67 hips. In the remaining six patients, one re-revision surgery was necessary to eradicate the infection; re-revisions included debridement and retention ($n=2$) or

Table 1
Patients characteristics.

Parameter	Value
Number of patients (hips; [n])	94 (97)
Age at primary THA (years)	59 ± 10.8 (19–84)
Age at first stage revision THA (years)	67 ± 11.8 (21–86)
Time between primary THA and first stage revision (years)	9 ± 7.9 (0.3–32)
Side (n; [% right])	39 (40)
Gender (n; [% female])	25 (27)
Primary bacteremia (n; %)	22 (23)
Other primary focus of infection (n; %)	5 (5)
Rheumatoid arthritis (n; %)	12 (12)
Psoriasis (n; %)	0 (0)
Gout (n; %)	5 (5)
Diabetes (n; %)	20 (21)
Malignancy (n; %)	3 (3)
Immune deficiency (n; %)	4 (4)
Congestive heart failure (n; %)	18 (19)
Renal failure (n; %)	21 (22)
Liver cirrhosis (n; %)	2 (2)
Corticosteroids (n; %)	8 (8)
Chemotherapy (n; %)	1 (1)
IV drug abuse (n; %)	2 (2)
Alcoholism (n; %)	10 (10)
Smoking (n; %)	13 (13)
BMI > 30 (n; %)	24 (25)
Persistent infection (n; %)	6 (6)
Functional failure (n; %)	16 (17)

Table 2
Medical history of patients with functional failure.

No	Sex	Age primary THA (years)	Aseptic revision	Age aseptic revision (years)	Age PJI (years)	Functional failure	Risk factors
1	Female	68	None		74	Girdlestone	BMI > 30, smoking, cardiac insufficiency
2	Male	64	None		75	Girdlestone	BMI > 30, smoking, alcohol misuse, gout, cardiac insufficiency, renal insufficiency
3	Male	42	Periprosthetic fracture (A1), ORIF	47	47	Girdlestone	BMI > 30, smoking, diabetes
4	Male	58	None		62	Girdlestone	None
5	Male	62	None		64	Girdlestone	BMI > 30
6	Male	62	Cup exchange	76	77	Girdlestone	None
7	Male	59	None		61	Girdlestone	Alcohol misuse
8	Male	49	THA exchange	71	86	Girdlestone	BMI > 30, diabetes
9	Male	57	None		60	Girdlestone	BMI > 30, alcohol misuse, diabetes, cardiac insufficiency
10	Female	83	None		86	Girdlestone	BMI > 30, renal insufficiency
11	Male	58	None		59	Girdlestone	BMI > 30, smoking, diabetes
12	Male	61	THA exchange	79	83	Girdlestone	Renal insufficiency
13	Male	51	THA exchange	75	76	Disarticulation	BMI > 30, smoking, alcohol misuse, diabetes, cardiac insufficiency, renal insufficiency
14	Male	69	None		71	Girdlestone	None
15	Male	66	THA exchange	69	69	Girdlestone	BMI > 30, smoking, chronic cortisone treatment
16	Male	52	Periprosthetic fracture (C), ORIF	81	84	Girdlestone	Cardiac insufficiency

two-stage revision ($n=4$). In 5 hips, long-term antibiotic suppression was initiated, due to persisting infection after the initial two-stage revision ($n=3$) or re-revision ($n=2$). In 15 hips, a definitive Girdlestone situation procedure had to be performed, due to persisting infection (Table 2). In seven hips, the Girdlestone procedure was performed after failure of the initial PJI treatment. In seven hips, the Girdlestone procedure was performed after failure of one ($n=5$) or two ($n=2$) re-revisions for a persisting infection. In 14 hips, the Girdlestone situation resulted in infection freeness. In one patient, infection persisted despite Girdlestone situation, requiring long-term suppression antibiotic treatment. One hip required hip disarticulation due to uncontrollable infection after the initial two-stage revision. Three patients (three hips) died during the follow-up period with no sign of a persistent infection and four patients (four hips) died during the 12 weeks of antibiotic treatment. Two patients (two hips) were lost to follow-up.

Patients with a BMI > 30 and patients who smoked, demonstrated higher rates of functional failures. The rate of functional failure stood at 10 out of 24 for adipose patients and 6 out of 13 for patients who smoked (Fisher's exact test: $p=0.001$ and $p=0.01$). In contrast, the rate of persisting infections stood significantly lower at 3 out of 24 ($p=0.336$) for patients who were adipose and 1 out of 13 ($p=0.587$) for patients who smoked.

3.3. Survival

Kaplan-Meier showed an overall cumulative survival rate of 80.4% (S.E 4%) of the definitive implant, at a follow-up time of 5 years (Fig. 1). These patients showed successful eradication of infection and presented with a functional implant throughout the follow-up period.

Obese patients with BMI ≥ 30 and patients who smoked demonstrated a significantly lower survival of 60.9% (S.E 1%) and 50.6% (S.E 1.4%), respectively at 5 years ($p=0.001$) (Fig. 1b). Eradication of infection was achieved in 93.3% (S.E 2.9%) and there were no differences between obese and non-obese as well as smokers and non-smokers found, respectively (Fig. 2).

3.4. Multivariate Cox-Regression

Out of the 16 independent variables, that were entered into a cox-regression analysis with either infection free survival and/or

functional survival as endpoints (Table 2), Only three variables (obesity, smoking, and alcoholism) showed to influence the overall survival, with a hazard ratios (HR) of 4.92, 3.97, and 7.76, respectively.

Considering infection eradication exclusively precluded all three factors as influential factor (Table 3).

4. Discussion

This study demonstrated an increased risk of conversion to a Girdlestone situation or amputation, in obese patients (BMI ≥ 30) and smokers, undergoing two-stage revision for hip PJI.

This study revealed an eradication rate of 93%. However, Infection-free functional survival rate stood at 80%, 5 years after revision. These values are comparable to recent reports [16–19].

The past two decades revealed no major advances in two-stage revision surgeries [20–24]. Eradication rates have consistently been shown to be high. However, less emphasis was put on, the more pronounced, functional failure. It is fair to emphasize the need to identify factors influencing not only the eradication of infection, but also the functional survival of the implant.

Obesity has previously been identified as a risk factor for both primary and revision hip arthroplasty, including two-stage revision for PJI [25].

The novelty of this study lies in the results, which draw attention to the fact that obesity and smoking are controllable factors likely to influence the likelihood of conversion to a Girdlestone situation or amputation.

The findings of the study indicate that abstinence from smoking, alongside weight control may both provide beneficiary effects on the outcome of two-stage hip revision in PJI. Abstinence from smoking could be safely performed during any stage of the treatment. The question whether weight loss should be advocated during a two-stage treatment process arises, since weight loss prior to primary arthroplasty have been linked to inferior outcome in general [12]. Whether this applies to two-stage procedures is unknown. The reality is that once PJI strikes, the problem is present and the risk has to be dealt with. It is still safe to postulate that based on the results of this study, nutritional support and abstinence from smoking are likely to be of benefit during two-stage treatment of hip PJI.

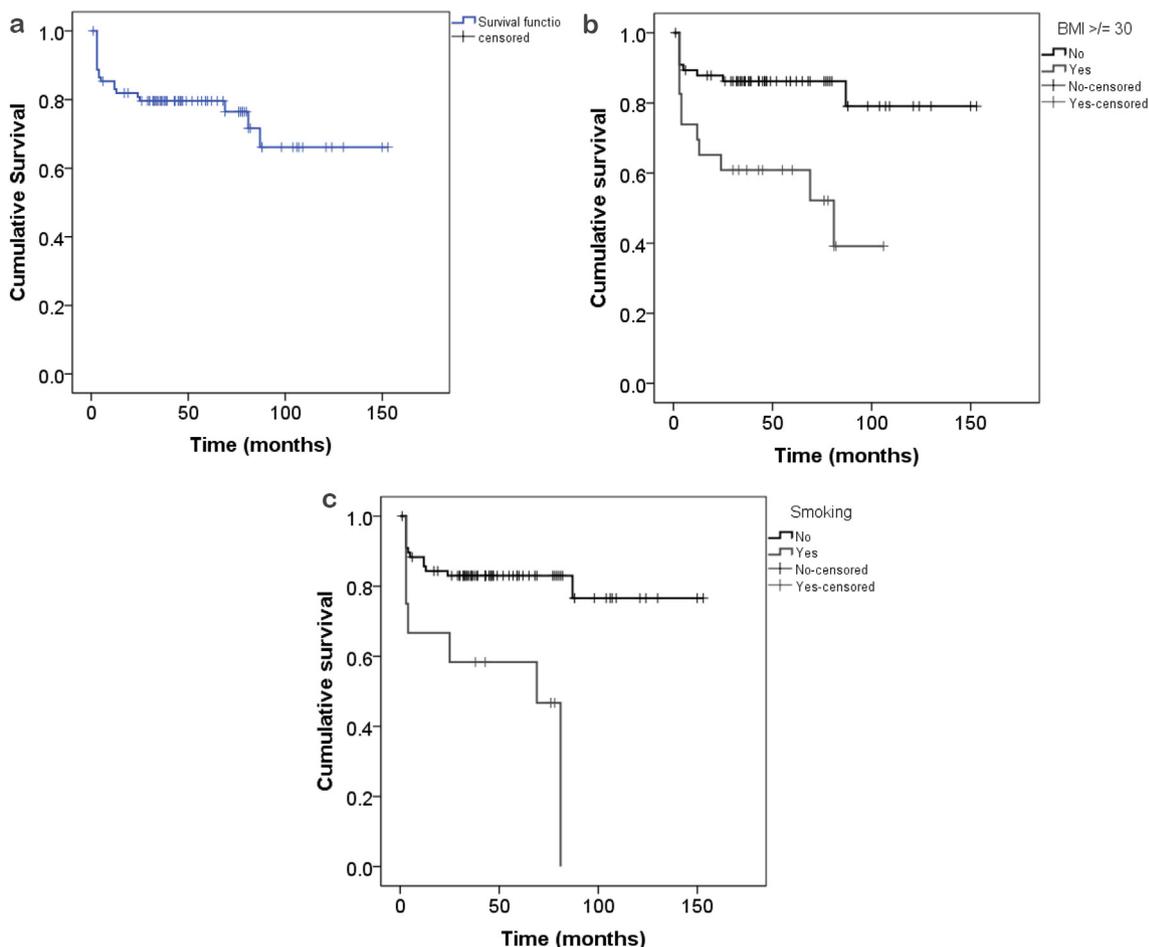


Fig. 1. a: cumulative overall Kaplan-Meier survival; b: overall cumulative Kaplan-Meier survival of obese vs. non-obese (log rank $p < 0.001$); c: overall cumulative Kaplan-Meier survival of smokers vs. non-smokers (log rank $p < 0.001$).

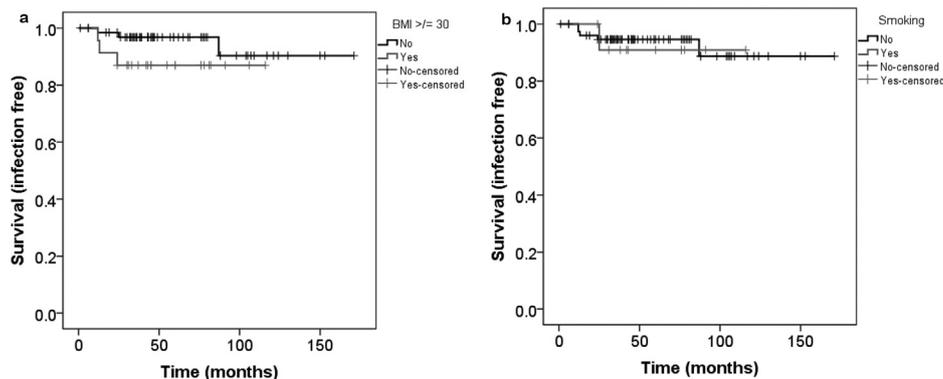


Fig. 2. a: overall cumulative Kaplan-Meier infection free, obese vs. non-obese (log rank non-significant n.s.); b: overall cumulative Kaplan-Meier infection free, of smokers vs. non-smokers (log rank n.s).

A limitation of this study is its retrospective nature with the indelible limitations of such a study design, such as selection bias. Furthermore, patients might have benefited from improved techniques acquired over time. Due to the variable functional results following articulating antibiotic-impregnated hip spacer in some patients, the standardised interval between stages varied since the first case included in the study. As a result, this might have affected the success rates following septic revision hip arthroplasty. We tried to minimize such biases with practice by surgeons from the same department. Furthermore, the study

included a relatively large series of patient with a long follow up.

It can be concluded that obesity and smoking are factors determining infection free survival in two-stage revision hip arthroplasty. The likelihood of conversion to a Girdlestone situation or even an amputation is increased in this subgroup of patients. Clinicians should be aware of the potentially devastating fate of the joint and should discuss the risks with the patients early during treatment. Abstinence from smoking and nutritional advice may be preventative measures, during the window of antibiotic treatment.

Table 3
Cox regression analysis.

Co-morbidity	Persistence of infection (PI)				Functional failure (FF)				PI or FF			
	HR	5% CI	95% CI	p-value	HR	5% CI	95% CI	p-value	HR	5% CI	95% CI	p-value
Primary bacteremia	0.00	0.00		0.971	1.65	0.45	6.08	0.456	1.18	0.34	4.01	0.798
Other primary focus of infection	> 10 ³	0.00	> 10 ³	0.940	1.01	0.06	17.21	0.995	1.08	0.12	9.90	0.945
Rheumatoid arthritis	2.78	0.14	56.31	0.506	0.00	0.00		0.981	1.03	0.12	8.56	0.978
Gout	> 10 ³	0.00	> 10 ³	0.929	0.15	0.01	4.37	0.272	0.21	0.12	3.57	0.281
Diabetes	0.48	0.03	8.46	0.616	0.41	0.89	1.85	0.244	0.29	0.69	1.18	0.083
Malignancy	> 10 ³	0.00		0.983	0.00	0.00		0.991	0.00	0.00		0.993
Immune deficiency	0.00	0.00		0.986	0.00	0.00		0.978	0.00	0.00		0.983
Congestive heart failure	0.00	0.00	> 10 ³	0.897	0.88	0.29	3.43	0.858	0.61	0.16	2.37	0.473
Renal failure	4.47	0.00	> 10 ³	0.995	0.68	0.15	3.05	0.615	0.49	0.11	2.14	0.344
Liver cirrhosis	0.06	0.00		0.999	2.24	0.00		1.000	0.00	0.00		0.996
Corticosteroids	> 10 ³	0.00	> 10 ³	0.942	0.48	0.05	5.04	0.543	0.83	0.14	4.77	0.831
Chemotherapy	0.38	0.00		1.000	0.00	0.00		0.994	0.00	0.00		0.996
IV drug abuse	2.45	0.00		1.000	0.00	0.00		0.995	0.00	0.00		0.996
Alcoholism ^a	154.07	0.00	> 10 ³	0.982	4.36	0.71	26.70	0.111	7.76	1.47	40.97	0.016
Smoking ^a	0.00	0.00	> 10 ³	0.925	4.01	1.04	15.57	0.045	3.97	1.08	14.65	0.038
BMI > 30 ^a	> 10 ³	0.00	> 10 ³	0.937	4.27	1.29	14.13	0.017	4.92	1.63	14.82	0.005

^a Included in multivariate analysis.

Disclosure of interest

The authors declare that they have no competing interest.

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Contributions of authors

S.S. Ahmad and F.M. Klenke equally contributed to the conception and design of the research; S.S. Ahmad and F.M. Klenke contributed to the acquisition and analysis of the data; S.S. Ahmad, L. Orlik, S.J.S. Ahmad, C.E. Albers, K.A. Siebenrock and F.M. Klenke contributed to the interpretation of the data; S.S. Ahmad and F.M. Klenke drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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