Original Research

Hypertension and low cholesterol as risk factors for infection after primary inflatable penile prosthesis surgery

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Abstract

Background: Inflatable penile prosthesis (IPP) is an effective surgical intervention in the treatment of erectile dysfunction. However, infection is a devastating complication of IPP placement. We sought to evaluate the association between medical comorbidities, medications, and serum metabolic lab values, and infection following primary IPP placement in our ethnically diverse population. **Methods**: A retrospective chart review was performed on all men who had primary IPP placement between 2017–2019 at our institution. Variables collected included patient demographics, medical history, medication usage, and pre- and postoperative lab values, within six months of surgery, including hemoglobin A1c, total cholesterol, and low density lipoprotein. Rates of postoperative infection through 60 days were noted. Patients were grouped either into the infected or non-infected cohort based on postoperative infection status. A Student's unpaired *t*-test was used to compare numerical variables and a Pearson chi-square test or Fisher's exact test was used to compare categorical variables between the cohorts. **Results**: A total of 293 men underwent primary IPP placement, of whom 14 (4.8%) were in the infected cohort and 279 (95.2%) in the non-infected cohort. The infected cohort was more likely to have a history of hypertension (92.9% vs 74.2%, $p = 0.026$) and statins medication usage (78.6% vs 52.0%, $p = 0.039$) when compared to the non-infected cohort, respectively. The infected cohort had a significantly lower postoperative cholesterol value (136.3 mg/dL vs 170.0 mg/dL, $p = 0.024$) and postoperative low density lipoprotein (LDL) value (65.2 mg/dL vs 92.1 mg/dL, $p = 0.020$) when compared to the non-infected cohort, respectively. **Conclusions**: Hypertension and usage of statin medications were more common in men who developed infection following IPP placement. As hypertension can disrupt microvasculature over time, it may contribute to poor healing post-IPP placement. Future research is warranted to determine statins' anti-inflammatory effect on wound healing and ability to fight infection.

Keywords: erectile; implant; prosthesis; infection; inflatable; risk

1. Introduction

Erectile dysfunction (ED) represents a complex clinical entity with a multifactorial etiology, including cardiovascular disease, psychosocial status, and lifestyle factors such as obesity and lack of physical exercise [1,2]. Additionally, ED has been found to have a profound effect on both quality of life and economic status; men with ED report substantially lower physical and mental health scores [3].

Penile prosthesis surgery represents a safe and durable treatment modality in patients with refractory ED. Although satisfaction rates are difficult to evaluate, penile prosthesis surgeries are associated with high patient satisfaction [4]. In the United States, it is estimated that approximately 25,000 inflatable penile prosthesis (IPP) procedures are done on a yearly basis [5]. Despite its success, infection remains a particularly devastating complication of IPP placement and can range between 0.3 to 11.4%, and as high as 15% in those with Peyronie's Disease [6–8].

Given the significant risk of infection in IPP placement, there is a need for further identification of trends and risk factors contributing to implant infection. Thus, we aimed to delineate factors associated with infection after primary IPP surgery in a highly comorbid, diverse patient population.

2. Materials and methods

Following Institutional Review Board approval (protocol #2021-13240), all IPPs placed at a single tertiary academic medical center by a single surgeon between 2017–2019 were retrospectively reviewed. The following data was abstracted: patient demographics, medical history, and pre- and postoperative labs including hemoglobin A1c, low density lipoprotein (LDL), and total cholesterol within six months of the surgery. Urine cultures were obtained within 30-days preoperative. Sixty-day postoperative course was reviewed for infection, which was defined as an infection requiring antibiotics and/or surgical removal or revision of the IPP [9]. Hypertension was defined as systolic blood pressure values of 130 mmHg or more and/or diastolic blood pressure more than 80 mmHg.

For those who developed a postoperative infection, the causative organism, antibiotic regimen prescribed, and surgical management were abstracted. Exclusion criteria included patients who had revision IPP surgery, IPP replacement, non-primary IPP, or malleable prosthesis insertions. All primary IPPs were placed through a penoscrotal incision and consisted of the Coloplast three-piece IPP soaked in a mixture of gentamicin and rifampin in accordance with our local antibiogram.

Patients were grouped into one of two cohorts based postoperative infection status: infected cohort or non-infected cohort. Data was analyzed using IBM SPSS version 27 (Chicago, IL, USA). Student's unpaired t-test was used to compare numerical variables between cohorts. Pearson chi-square test or Fisher's exact test was used to compare categorical variables between cohorts. p-values less than 0.05 were considered statistically significant.

3. Results

A total of 293 primary IPP surgeries were performed at our institution, with 14 (4.8%) men in the infected cohort and 279 (95.2%) men in the non-infected cohort. The majority of men in both cohorts were of Hispanic race/ethnicity (78.6% infected cohort vs 74.9% non-infected cohort) and had a medical history significant for diabetes mellitus (64.3% infected cohort vs 57.7% non-infected cohort). A significantly greater percentage of men in the infected cohort had a history of hypertension (92.9% vs 74.2%, p = 0.026) and were on statins (78.6% vs 52.0%, p = 0.039) when compared to men in the non-infected cohort, respectively (Table 1).

All patients (100%) who had an IPP infection were successfully treated with antibiotics, removal of the IPP, and replacement with a malleable implant. For men who developed a postoperative infection, the average time from surgery to infection was 42.9 ± 19.9 days (range: 14–77 days) and the average time from infection presentation (either to the clinic or emergency department) to surgical revision was 3.2 ± 6.2 days (range: 0–24 days). Postoperative wound cultures obtained from the wound site at the time of IPP replacement identified several organisms, most commonly Methicillin-Resistant Staphylococcus Aureus (MRSA) (35.7%), Escherichia coli (E. coli) (21.4%), and normal skin flora (21.4%) (Fig. 1).

The infected cohort had a significantly lower postoperative cholesterol value (136.3 mg/dL) when compared to the non-infected cohort (170.0 mg/dL, p = 0.024). Additionally, the infected cohort had a significantly lower postoperative LDL value (65.2 mg/dL) when compared to the non-infected cohort (92.1 mg/dL, p = 0.020). There were no significant differences in pre- and postoperative hemoglobin A1c, and preoperative cholesterol and LDL values between the cohorts (p > 0.05) (Table 2).

Of the men with hypertension, there were no significant differences in infection rates between those who were

Table 1. Patient demographics and comorbidities.

	Non-infected	Infected	p-value
	N = 279	N = 14	
Age, years, mean (SD)	63.4 (8.5)	61.2 (7.9)	0.334
Race/Ethnicity, n (%)			n/a
Hispanic	209 (74.9)	11 (78.6)	
Non-hispanic white	1 (0.4)	0 (0)	
Non-hispanic black	0 (0)	0 (0)	
Others/Declined	69 (24.7)	3 (21.4)	
Body mass index, mean (SD)	28.9 (4.7)	30.1 (6.9)	0.522
Smoking status, n (%)			0.095
Current smoker	27 (9.7)	4 (28.6)	
Former smoker	75 (26.9)	3 (21.4)	
Never	177 (63.4)	7 (50.0)	
Marital status, n (%)			0.324
Single	67 (24.0)	4 (28.7)	
Married	106 (38.0)	8 (57.1)	
Divorced	38 (13.6)	1 (7.1)	
Other/Declined	68 (24.4)	1 (7.1)	
Medical history, n (%)			
Diabetes mellitus	147 (57.7)	9 (64.3)	0.409
Hypertension	207 (74.2)	13 (92.9)	0.026*
Chronic kidney disease	32 (11.5)	2 (14.3)	0.780
End stage renal disease	3 (1.1)	0 (0)	0.083
Peyronies disease	24 (8.6)	2 (14.3)	0.573
Coronary artery disease	30 (10.8)	4 (28.6)	0.182
Prostatectomy	67 (24.0)	2 (14.3)	0.340
Medication usage, n (%)			
Insulin	50 (17.9)	6 (42.9)	0.08
Oral antiglycemics	119 (42.7)	9 (64.3)	0.134
Antihypertensives	202 (72.4)	12 (85.7)	0.206
Statins	145 (52.0)	11 (78.6)	0.039*

*p-value is statistically significant ($p < 0.05$).

taking antihypertensive medications (6.3%) and those who were not taking antihypertensive medications (7.1%, p = 0.897). Additionally, of the men with normal baseline cholesterol (less than 200 mg/dL), there were no significant difference in infection rates between those who were taking statins (5.5%) and those who were not taking statins (5.3%, p = 0.976).

4. Discussion

We evaluated the correlation between medical comorbidities, medications, and serum metabolic lab values, and IPP infection. Our findings suggest that in our highly comorbid, ethnically diverse population, a history of hypertension and usage of statin medications were more common among men who developed an infection after IPP placement when compared to those who did not. Furthermore, according to the knowledge of the authors, our single-center retrospective experience is the first to show that lower postoperative cholesterol and LDL levels were more likely to be found in men with postoperative IPP infection.

Despite improved standards and techniques in maintaining sterility, such as the "No-Touch" surgical technique [10], infection remains one of the most feared complica-
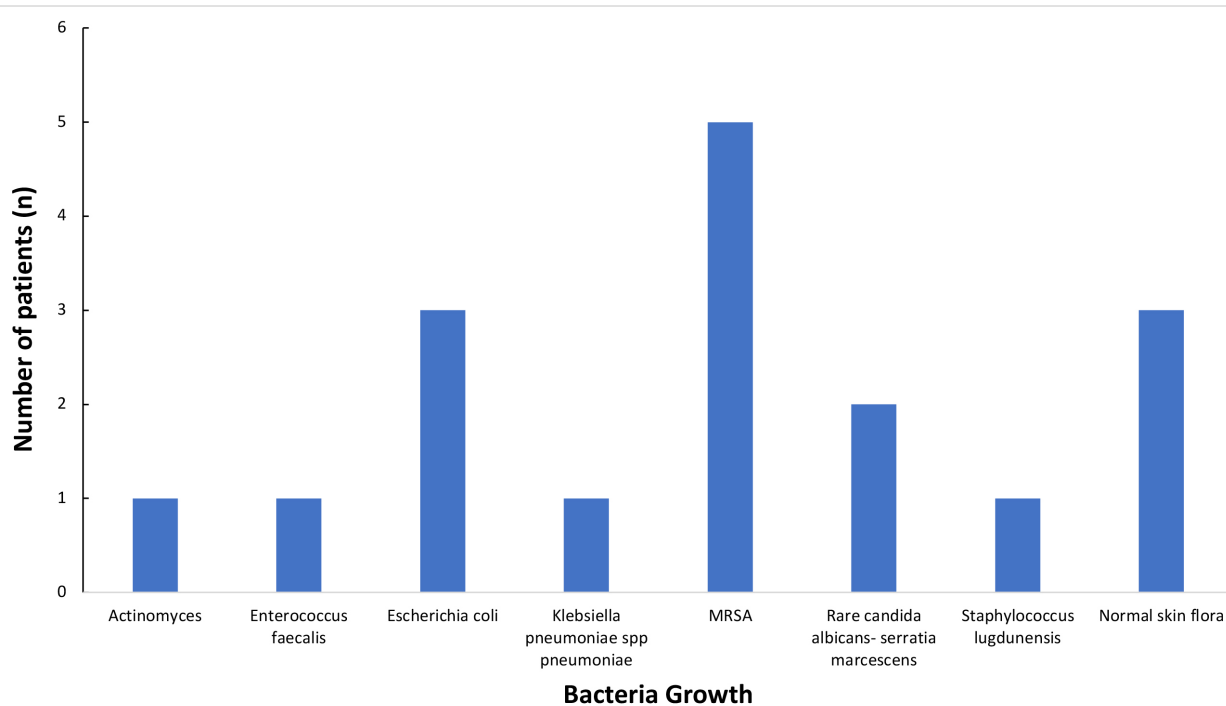
Fig. 1. Wound culture bacterial growth of infected patients after IPP placement. MRSA, Methicillin-Resistant Staphylococcus Aureus.

Table 2. Patient pre- and post-operative lab values.

	Non-infected	Infected	p-value
Preoperative hemoglobin A1c, %, mean (SD)	7.0 (1.4)	8.3 (1.7)	0.115
Postoperative hemoglobin A1c, %, mean (SD)	7.1 (1.8)	8.1 (1.7)	0.108
Change in hemoglobin A1c, %, mean (SD)	0.3 (1.5)	–0.3 (0.3)	0.340
Preoperative cholesterol, mg/dL, mean (SD)	164.0 (45.0)	160.6 (48.2)	0.883
Postoperative cholesterol, mg/dL, mean (SD)	170.0 (47.8)	136.3 (26.2)	0.024*
Change in cholesterol, mg/dL, mean (SD)	3.3 (32.9)	4.0 (20.0)	0.95
Preoperative low-density lipoprotein, mg/dL, mean (SD)	88.9 (38.8)	90.5 (34.7)	0.932
Postoperative low-density lipoprotein, mg/dL, mean (SD)	92.1 (44.5)	65.2 (18.1)	0.020*
Change in low-density lipoprotein, mg/dL, mean (SD)	6.8 (34.0)	0 (0)	0.941

*p-value is statistically significant ($p < 0.05$).

tions of penile implant surgery. This holds true for both malleable and inflatable implants, where some reports have suggested the incidence of infection to be as high as approximately 9% [11]. When evaluating for specific risk factors associated with implant infection, Carjaval *et al.* [12] conducted a systematic review and meta-analysis of over 175,000 patients who underwent penile prosthesis implantation, and found that diabetes mellitus and immunosuppression were associated with increased infection rates whereas primary surgery and strategies to promote sterility, such as coating the implant with infection-retardant materials, were associated with reduced infection rates. Interestingly, in our study, despite the increased prevalence of diabetes mellitus in both cohorts, we did not observe diabetes mellitus or hemoglobin A1c levels to be associated with increased rates of infection. Furthermore, in addition to pre-

operative risk factors, there are also intraoperative risk factors such as the surgical approach used for IPP placement. Generally, IPPs are placed using penoscrotal, infrapubic, or subcoronal incisions. IPP placement through a subcoronal incision generally has a longer operative time and therefore may increase the risk of infection. However, the current data is limited to confirm this hypothesis [13].

A large multicenter retrospective study aimed to identify the microorganisms involved in penile prosthesis infection. By reviewing intraoperative cultures obtained at explantation (from the purulent material in the implant space and biofilm present on the implant), Gross *et al.* [14] found both Gram positive and negative organisms in the positive cultures (73% and 39%, respectively). Additionally, nearly one-third of the cultures were found to harbor Candida, anaerobes, and Methicillin-Sensitive Staph Aureus

(MSSA). Conversely, in our study, the most common organisms identified were MRSA followed by E. coli and normal skin flora. Given differences in bacterial prevalence and resistance between different medical facilities, local knowledge of one's institutional antibiogram is essential to optimize timely and appropriate treatment of these infectious complications.

History of hypertension and usage of statins are not routinely studied as risk factors associated with infection following IPP surgery. It has been shown that chronically elevated blood pressure often elicits structural abnormalities in both the micro- and macrovasculature [15]. Therefore, it is plausible that damage to the vascular endothelium causing endothelial dysfunction may play a role in increasing risk for infection, especially in the setting of implanting a foreign object into a highly vascularized structure such as the penis.

Conversely to hypertension, low levels of cholesterol and LDL have been associated with delaying atherosclerotic progression [16]. Given the presumed benefits of lower cholesterol values and statin medications in physical function and survival [17], our findings of significantly lower cholesterol and higher use of statin drugs in patients who experienced an IPP infection is novel. Cholesterol has been shown to play a role in wound healing, with *in vivo* studies suggesting that inhibition of molecular healing networks enriched with cholesterol and fatty acid biosynthetic processes results in delayed wound healing and persistent unresolved inflammation [18]. Interestingly, in nonurologic surgeries (ex: gastrointestinal surgery), serum total cholesterol levels less than 160 mg/dL have been shown to be associated with increased incidence of superficial and deep surgical skin infections [19]. This may be as a result of low serum cholesterol translating to decreased circulating lipoproteins, which play a role in antibacterial and anti-inflammatory pathways [20]. Furthermore, statins, the most commonly prescribed class of anti-cholesterol drug, have been shown to have anticoagulant and antiproliferative properties that may influence wound healing [21]. Statins have also been shown to have immunomodulatory effects through inhibition of the rate limiting enzyme in pathways of the immune response and therefore suppressing immune cell activation and migration, cytokine production, and immune metabolism and survival [22]. Therefore, we postulate that in the setting of IPPs, statin use may contribute to inhibiting the immune response subsequently making patients more vulnerable to implant infection.

This study is not without limitations. First, the retrospective nature introduces several biases including inaccurate and incomplete capture of data, and inability to control for variables such as medication adherence. Second, our sample size for the infected cohort is limited and we may see different results with a larger sample size. Third, lab values were obtained at unstandardized intervals during the pre- and postoperative period, possibly limiting the utility of these parameters. Despite these limitations, although the findings of this study do not directly identify a causal relationship between hypertension, statin medication usage, and low postoperative LDL and cholesterol, and IPP infections, they do shed light on differences between men who did and did not experience infection following primary IPP placement.

5. Conclusions

Despite strides in its prevention, IPP infection continues to be a significant problem in prosthetic surgery. The novel findings of this study suggest that hypertension, statin medication usage, and lower postoperative LDL and cholesterol levels were more common amongst patients who develop an IPP infection. Prospective, multicenter studies with larger sample sizes are warranted to confirm the findings of this study.

Author contributions

DM, KW, and PM designed and supervised the study. JL and CR collected the data. CR analyzed the data. JL, JM, CR, MB, KW, DM, PM prepared the manuscript and figures. All authors approved the submitted manuscript.

Ethics approval and consent to participate

The institutional review board of the Albert Einstein College of Medicine approved of this study under protocol # 2021-13240.

Acknowledgment

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

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