

# Preoperative Hyaluronic Injections Are Not Associated with Periprosthetic Joint Infection Following Unicompartmental Knee Arthroplasty

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## INTRODUCTION:

Limited research exists on periprosthetic joint infection (PJI) risk in unicompartmental knee arthroplasty (UKA) patients receiving preoperative hyaluronic acid (HA) injections. This study examines whether HA injections are associated with increased PJI risk and if the timing of injections plays a role.

## METHODS:

The PearlDiver administrative claims database was queried to identify patients who underwent UKA between 2010 and 2023. Patients receiving ipsilateral HA injections within one year prior to surgery were grouped into <3 months and 3–12 months. A control cohort of patients who did not receive an injection within the year preceding UKA were matched to the injection cohort based on age, sex, Charlson Comorbidity Index (CCI), tobacco use, diabetes, and obesity. Univariable and multivariable analyses, including logistic regression, evaluated the association between HA injections and PJI one year postoperatively.

## RESULTS:

A total of 6,132 UKA patients with HA injections <3 months and 1,519 with injections 3–12 months before surgery, were matched to 6,934 controls without HA or corticosteroid injections one year before surgery. There were no significant differences in PJI risk among patients who received HA at <3 months (OR 0.61, 95% CI: 0.40–0.94; p = 0.075) or 3–12 months (OR 0.93, 95% CI: 0.50–1.73; p = 0.075). Multivariate analysis revealed that neither HA injections at <3 months (OR 0.89, p = 0.611) or HA injections at 3–12 months (OR 1.49, p = 0.209) were associated with increased PJI risk after adjusting for age, CCI, CHF, asthma, complicated diabetes, CKD, hypothyroidism, and obesity.

## DISCUSSION AND CONCLUSION:

Patients who received HA injections within 3 months preoperatively did not demonstrate an increased odds of developing PJI relative to patients without injections or those receiving injections greater than 3 months before surgery. No significant differences in PJI risk were observed with HA administration at any time point up to one year preoperatively.

**Table 1. Patient demographics**

% of total (absolute number)	Injections <3 months before surgery (n=6132)	Injections 3-12 months before surgery (n=1519)	Never injections (n=6934)	P-value
Age (mean, SD)	67.1 (10.2)	67.6 (10.2)	67.1 (10.1)	0.786
Male gender	2,643 (43.1%)	656 (43.2%)	2,987 (43.2%)	0.857
CCI (mean, SD)	1.56 (1.8)	1.52 (1.8)	1.54 (1.8)	0.762
Smoking	483 (7.9%)	214 (14.1%)	154 (2.2%)	0.303
Comorbidities				
Asthma	1,319 (21.5%)	333 (21.9%)	1,047 (15.1%)	0.135
Cancer	1,459 (23.8%)	452 (29.8%)	1,097 (15.8%)	0.282
CHF	1,867 (30.5%)	449 (29.6%)	1,179 (17.0%)	0.396
CKD	475 (7.7%)	171 (11.3%)	101 (1.5%)	0.048
CompD	1,486 (24.2%)	339 (22.3%)	1,450 (20.9%)	0.440
Diabetes	461 (7.5%)	101 (6.6%)	1,048 (15.1%)	0.008
Hypertension	3,844 (62.5%)	974 (64.2%)	2,221 (31.9%)	0.280
Obesity	1,122 (18.3%)	309 (20.3%)	1,048 (15.1%)	0.132
Compensation	3,844 (62.5%)	974 (64.2%)	2,221 (31.9%)	0.280
Diabetes	1,411 (23.0%)	317 (20.9%)	1,422 (20.5%)	0.430
Hypertension	1,254 (20.4%)	401 (26.4%)	764 (11.0%)	0.440
Liver Disease	1,182 (19.3%)	284 (18.7%)	1,318 (19.0%)	0.886
Obesity	1,176 (19.2%)	302 (19.9%)	1,064 (15.3%)	0.173
Biomarkers				
AChE	483 (7.9%)	131 (8.6%)	178 (2.5%)	0.492

CCI, Charlson Comorbidity Index; CHF, chronic heart failure; CKD, chronic kidney disease; CompD, chronic obstructive pulmonary disease; SD, standard deviation.

**Table 2. Primary end point**

% of total (absolute number)	Injections <3 months before surgery (n=6132)	Injections 3-12 months before surgery (n=1519)	Never injections (n=6934)	P-value
PJI	132 (2.1%)	131 (8.7%)	39 (0.6%)	0.075

<sup>a</sup>Patients assigned to a single time group based on the nearest administration injection.

**Table 3. Multivariable ORs in timing of HA injections**

Exposure	n (absolute)	Odds Ratio	95% Confidence Interval	P-value
<3 Months	4,822 (77)	1.73	0.86-2.14	0.107
3-12 Months	1,861 (19)	1.74	0.61-1.94	0.142
3-12 Months	477 (23)	1.70	0.85-2.14	0.109
6-12 Months	556 (35)	1.49	0.72-2.97	0.066
6-12 Months	305 (20)	1.73	0.82-2.39	0.087

<sup>a</sup>Patients assigned to a single time group based on the nearest HA administration.

**Table 4. Univariable predictors of infection**

% of total (absolute number)	Infected UKA (n=199)	Non-infected UKA (n=71,449)	P-value
Timing of HA Injections			
<3 Months	81 (40.7%)	4,306 (6.0%)	0.004
3-12 Months	12 (6.0%)	1,597 (2.2%)	0.219
6-12 Months	39 (19.3%)	4,705 (6.6%)	0.102
Age (mean, SD)	67.52 (10.14)	67.11 (10.21)	0.154
Sex	103 (51.8%)	1,946 (27.2%)	0.130
CCI (mean, SD)	1.67 (1.8)	1.58 (1.78)	0.002
Smoking	20 (10.0%)	1,008 (14.1%)	0.132
Comorbidities			
Asthma	24 (12.1%)	1,530 (21.3%)	0.004
Cancer	11 (5.5%)	1,077 (15.1%)	0.335
CHF	30 (15.1%)	1,424 (20.0%)	0.319
CKD	20 (10.1%)	1,548 (21.7%)	<0.001
CompD	21 (10.5%)	1,310 (18.3%)	0.004
Diabetes	26 (13.1%)	1,076 (15.0%)	0.118
Hypertension	20 (10.0%)	1,536 (21.4%)	0.002
Obesity	16 (8.0%)	1,475 (20.6%)	0.118
Biomarkers			
AChE	17 (8.5%)	1,030 (14.4%)	0.019
Hypertension	30 (15.1%)	1,499 (21.0%)	0.006
Liver Disease	21 (10.5%)	1,461 (20.4%)	0.146
Obesity	21 (10.5%)	1,434 (20.0%)	0.001
Biomarkers	11 (5.5%)	1,171 (16.4%)	0.002

**Table 5. Multivariate predictors of infection**

% of total (absolute number)	Estimate	Standard Error	P-value
CCI (mean, SD)	0.027	0.047	0.443
Timing of HA Injections			
<3 Months	0.49	0.16-1.19	0.011
3-12 Months	1.49	0.76-2.66	0.200
Asthma	1.05	0.62-1.73	0.848
Comorbidities			
Compensation	1.40	0.79-2.41	0.234
Hypertension	1.78	1.18-2.54	0.004
Obesity	1.36	0.93-1.96	0.001

<sup>a</sup>Timing of HA Injections refers to presence of end-organ involvement (e.g., renal disease, vitreous opacities).

<sup>b</sup>Patients assigned to a single time group based on the nearest administration injection.

CCI, Charlson Comorbidity Index; CHF, chronic heart failure; CKD, chronic kidney disease; CompD, chronic obstructive pulmonary disease; SD, standard deviation.

PJI, periprosthetic joint infection.

OR, Odds Ratio; CI, Confidence Interval.

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