## Testosterone Replacement Therapy Increases Revision Rates of Anterior Cruciate Ligament Reconstruction with Two-Year Follow Up

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INTRODUCTION: While it has been well documented that anabolic steroid use and exogenous testosterone lead to higher rates of tendinous rupture among athletes and the general population, there is a total lack of studies exploring revision rates and other complications in for ACL reconstruction (ACLR) surgery. Testosterone replacement therapy (TRT) has increased dramatically over the past several decades in the 18-45-year-old male age group. With ACLR being the most common treatment option for ACL injury, this study is extremely relevant for the upcoming generation of young athletes, maturing fathers, and patients who hope to cosmetically change their physical appearance. This study seeks to evaluate the relationship between TRT usage and the rates of ACLR revision using a series of data analyses designed to account for cohort-matching and the duration of TRT usage.

## METHODS:

A retrospective cohort of ACLR patients from 2010 to 2022 was gathered using the PearlDiver All Payer Claims Database (MARINER) (PearlDiver Technologies, Colorado Springs, Colorado, USA). CPT, ICD-9/10 diagnosis, and ICD-9/10 procedure codes were used to identify the study cohort, comorbidities, and outcomes. Patients with a history of ACLR, at least one year of prior appointments, and at least two years of follow-up were included for our study. Our experimental group of patients in this study additionally had a history of TRT use prior to ACLR with usage either defined as short-term (<90 days) or long-term (≥90 days). A total of three queries were conducted, our first one analyzing short-term usage of TRT with matched demographics (age, sex) and Charleston Comorbidity Index (CCI). Our second query accounted for long-term usage of TRT, did not match for comorbidities and demographics, and used multivariable analysis to determine the odds ratio for ACLR revision with TRT use. Finally, our third query included long-term TRT usage and additionally matched for comorbidities and demographics. For each query, univariate analysis using chi squared tests and student t-tests were used to compare demographics outcomes between groups. A Log-Rank test was used to compare overall survival rates between the groups.

## **RESULTS:**

Each query yielded results consistent with the others. Our first query (short-term TRT usage, matched cohorts) included sample sizes of n=2641 for both groups, with demographic matching for age (p=1.0), sex (p=1.0), and CCI (p=.44). The TRT group had a 6.36% incidence of ACLR revision while the control group had a 6.21% incidence, yielding no significant difference (p=.821). Our second query (long-term TRT usage, unmatched cohorts) included a sample size of n=114467 for the control group and n=474 for the TRT group with p<.001 for all comorbidities and demographics. This yielded a statistically significant difference with a 6.12% revision rate in the TRT group and a 9.16% revision rate in the control group (p=.022), but after using a multivariable analysis to identify significant predictors, TRT usage demonstrated an odds ratio of 3.77 (95% CI: 2.83-4.96; p<.001). Our final query (long-term TRT usage, matched cohorts) included n=465 for both groups, with demographic matching for age (p=.93), sex (p=.85), and CCI (p=.23). The TRT group had a 15.27% incidence of ACLR compared to the 4.30% in the control group, demonstrating a statistically significant difference (p<.001).

## DISCUSSION AND CONCLUSION:

Our study demonstrated that long-term TRT usage is significantly associated with increased revision rates of ACLR in demographic and comorbidity-matched populations. With the incidence of testosterone therapy rising for older men, male athletes, and populations seeking to change their physical appearance, this data is especially contemporarily relevant. Physicians should consider this data to guide treatment options when deciding to treat ACL injuries in populations that have a history of long-term TRT use. Each query ran had its own independent variations in limitations in terms of either sample size, statistical significance, or cohort matching, but the general trend of TRT use and revision rates is apparent. More studies should be conducted to evaluate the safety of TRT for patients undergoing reconstructive ligamentous and/or use tendinous used to be a surgeries.

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Demographics and Control NLLR groups Protect temperature of the personal NLLR groups Protect temperature of tem												Demographics and Comorbidities of TRT and control ACLR groups							Revision ACLR and complications between TRT and control groups								
Patient Demographic		TRT D		Control		a N pole		10497	,	Significant prec	ictors in multivari	able analysis of rev	ISION ACLK	Patient Demographic	TRT			Control		Univariate	TRT			Control			
		%	p-value	n	%	Average Age	41		-0.001	803			Odds Ratio	95% CI	p		0	%	p-value	0	%			*	p-value		5
Total	2641			2641		See.						TOT	3.77	3.03.4.06	+0.001	Total	465			465		Total	465			465	
Average Age	89.5			39.7		Mah		13.41 M.39	1001	54008	20.00	INI	3.77	2.63%.90	0.001	Mean age, yr	42.8		0.93	42.4		Breising ACLR	71	15.22	+1.001	20	4.30
Sex						Egoporation	290	94-07	1.065	1048	1.17	Osteoarthritis	1.16	1.08-1.26	<0.001	Sea			0.85			2407					
Female	351	13.29	1	351	13.29	Elaborati Television	10	34.34	<.001	50/14	5.11	Oberity	0.94	0.77.0.01	+0.001	female	73	15.70		75	16.13			0.00			
Male	2290	\$5.71	1	2290	86.71	Oncorthits	102	36.90	4.005	10500	11.60	Obesity	0.04	0.77-0.91	~0.001	Male	332	84.32		390	83.87	PE .	0	0.00		0	
Hypogenadism	464	17.57	<.001	66	2.50	Christis, Editory Zissaur	4	4.25	<001	60	0.60	age	0.95	0.95-0.95	< 0.001	Hypepanadism	249	53.55	<0.01	19	4.09	354	-1		-	-1	-
Dishetes	748	0.22	0.21	222	8.41	Consultant Inducts		40	1001	10.00	0.96					Diabetes	63	18.55	0.28	51	10.97	septic knee	-1			-1	
Tobarco Line	117	12.76	0.003	411	15.56	Dementia		4.25	1.005	28	0.08					Tobacco Lise	91	19.57	0.44	82	17.63						
Onternativitie		35.68	0.000	104	18.78	Excess shide		13.29	4.065	268	0.66					Orteosethelise	129	22.34	0.02	66	21.28						
Chargest Kidney Diseases		0.83	0.68	18	1.06	Berge Prestele Appropriate	10	6.33	1.065	80	0.80					Changie Eldoer Disease	-4										
circle soney ordered		0.07	0.40		2.00	Average CD Score	6.57		<.001	0.17						fleebel bloose		4.00	4.13		3.97						
AUCERICI ADUSE	01	2.31	0.12		2.59	Standard Cevahor Ry (1) 5094	10			0.4						Charles Advert		10.00	-0.05		12.47						
OBENS	346	11.00	0.005	241	9.15											Constra		10.94			14.47						
Congestive Heart Failure	15	0.57	0.32	21	0.80											Congessive Heart Failure	-1			-1							
Demerta	-1	-0.04	1	-1	-0.04											Lementia	-1			0	0.00						
Decreased Libido	122	4.62	<.001	- 44	1.67											Decreased Libido	52	11.18	<0.01	-1	-						
Erectile Dysfunction	179	6.78	<.001	97	3.67											Erectile Dysfunction	59	12.69	<0.01	23	4.95						
Benign Prostatic Hyperplasia	90	3.41	0.2	74	2.80											Benign Prostatic Hyperplasia	27	5.81	0.08	16	3.44						
Average CO Score	0.38		0.44	0.36												Average CCI Score	0.57		0.23	0.48							
Standard Deviation for CO Score	e 0.98			0.9												Standard Deviation for CEI Score	1.22			1.07							