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Testosterone Replacement Therapy and Rehospitalization in Older Men with Testosterone Deficiency in a Post-Acute Care Setting

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Abstract

Objective: To examine whether receipt of testosterone replacement therapy (TRT) was associated with reduced 30-day rehospitalization following Post-Acute-Care (PAC) among older men with testosterone deficiency.

Design, Patients and Methods: We conducted a retrospective cohort study using a 5% national sample of Medicare beneficiaries. We identified 1,290 nonsurgical inpatient PAC discharges between January 1, 2007 and October 31, 2014 for male patients, aged ≥ 66 years, with a prior diagnosis of testosterone deficiency. Multivariable logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for 30-day PAC rehospitalization related to receipt of TRT.

Results: In older men with testosterone deficiency, receipt of TRT was not associated with rehospitalization (odds ratio [OR]=0.87, 95% CI, 0.59-1.29) in the 30 days following PAC discharge. These findings persisted after adjustment for quintile of propensity scores (OR=0.90, 95% CI=0.62-1.30)

Conclusion: TRT was not associated with reduced rehospitalization following PAC discharge in older men with testosterone deficiency. Further research in this population should examine the effects of TRT on functional recovery and community independence.

Keywords

Androgen; Testosterone replacement therapy; Post-acute-care; Hospital readmission

INTRODUCTION

Testosterone deficiency is associated with significant decreases in lean muscle mass.¹ Illness or injury and prolonged inactivity can exacerbate this muscle loss in older men.^{2,3,4} Pharmacotherapy can also contribute to muscle loss in such patients. For example, glucocorticoids—frequently used for numerous inflammatory diseases—can trigger muscle loss and hypogonadism.⁵ In turn, muscle loss is associated with functional decline, loss of independence and repeated hospitalizations.⁶⁻⁹

Hypogonadism—defined by the Endocrine Society as having a total testosterone level <300 nanograms (ng) per deciliter (dL) and consistent signs and symptoms such as osteoporosis, muscle wasting, adiposity, low libido, fatigue and weakness¹—is reported to occur in 20% to 30% of men over the age of 60.¹⁰ Older men with hypogonadism are particularly susceptible to muscle loss and subsequent functional decline.¹¹ For these men, testosterone replacement therapy (TRT) may have a beneficial effect on lean tissue mass, bone structure, strength and overall functional health.¹²⁻¹⁴ It is possible that through these pathways TRT could reduce functional decline and decrease the risk for repeated hospitalizations in older men.

Rehospitalization has become a predominant quality indicator and has transformed healthcare delivery in recent years.¹⁵ Our previous study showed that TRT reduced the risk of risk of hospitalization 30 days following discharge.¹⁶ However, there are no large-scale studies assessing the effect of TRT on rehospitalization among older hypogonadal men following inpatient post-acute care (PAC), including skilled nursing (SNF) and inpatient rehabilitation facilities (IRF). Functional deficits are the primary indication for receiving PAC rehabilitation. Thus, this population may demonstrate particular benefits of TRT. We assessed whether TRT was associated with a reduced rate of 30-day rehospitalization following discharge from PAC in older men with hypogonadism.

PATIENTS AND METHODS

Study Design and Data Source

We conducted a retrospective cohort study using enrollment and claims data for a 5% national sample of Medicare beneficiaries. The Centers for Medicare and Medicaid Services selected these beneficiaries using the eighth and ninth digits (05, 20, 45, 70, 95) of patients'

health insurance claim numbers. These data files had variety of information including the patient's demographic and enrollment information (denominator file), claims for hospital stays (Medicare Provider Analysis and Review file), outpatient visits (Outpatient Standard Analytic file), Prescription Drug Event (PDE) records and physician services (Medicare carrier claim file). In our analysis, we used a methodology that is consistent with those used in previous studies of hospital readmission using national Medicare claims data.¹⁷⁻¹⁹ This study was reviewed and approved by the University of Texas Medical Branch Institutional Review Board (IRB). The IRB granted a waiver of informed consent for this investigation which relied on deidentified claims data. This study conforms to all STROBE guidelines and reports the required information accordingly (see Supplementary Checklist)

Study Cohort

We examined male Medicare beneficiaries who had at least one post-acute care (PAC) stay, whether IRF or SNF, between January 1, 2007 and October 31, 2014. For patients hospitalized multiple times during this period, we randomly selected one hospitalization per calendar year. To be included in the study patients were required to have met each of the following criteria: aged ≥ 66 years at PAC admission, a non-surgical diagnosis-related group, a diagnosis of hypogonadism (International Classification of Diseases, Ninth Revision, Clinical Modification, [ICD-9-CM] code=257.xx) in the 12 months prior to PAC admission, continuous enrollment in Medicare parts A, B, and D in the 12 months prior to PAC admission date, and no healthcare maintenance organization enrollment in the prior 12 months.

We defined a TRT user as a patient who has filled a prescription for TRT or received testosterone injection that extended at least until the patient's index PAC admission date. We included, in this definition, pharmacy fill dates of 30, 60, or 90 days before the index PAC admission date. We treated all TRT injections as the equivalent of a 30-day supply of a prescription TRT. We also included all doses and formulations of testosterone, using National Drug Code (NDC) numbers for topical gel, transdermal patch, subcutaneous pellets, and oral formulations (see Appendix) and Healthcare Common Procedure Coding System (HCPCS) codes for injectable formulations (see Appendix). We excluded patients who were discharged to another post-acute-care setting, including a rehabilitation facility, a skilled nursing facility, or a psychiatric hospital. We also removed patients who died during PAC stay or within 30 days of PAC discharge. In addition, based on the propensity score model, patients who were not in the propensity score overlap region were also removed.

Covariates

We obtained sociodemographic characteristics including age at index PAC stay, race and ethnicity (white, black, Hispanic, or other) using Medicare database. The two zip-code level variables, median household income, and proportion of persons aged ≥ 25 years in neighborhood with at least a high school education were obtained from Medicare data linked to 2011 American Community Survey estimates from the United States Census Bureau. Furthermore, we examined and adjusted for Elixhauser comorbidity score.²⁰

Outcome Assessment

We assessed all readmissions to an acute care hospital or critical access hospital within 30 days following discharge for the patient's index (PAC stay).

Statistical analysis

We used logistic regression models to estimate the association between TRT and all 30-day rehospitalizations following PAC. Multivariable analyses were adjusted for all demographic, clinical, and health services variables listed in Table 1. We also adjusted for the quintile of propensity score. We used the logistic regression model to estimate the propensity score with receipt of TRT as the binary outcome variable in 1,290 PAC admissions of men with testosterone deficiency. The propensity score model included all variables listed in Table 1. In the final models, we included patients whose propensity scores fell in the overlap region (99.7% of the cohort)

We then examined the distribution of the derived propensity score in the study cohort. We also checked the balance of each covariate according to receipt of TRT before and after adjustment of propensity score quintile as a covariate. Afterwards, we fitted the regression models adjusting for quintile of propensity score and for covariates that remained statistically significant after inclusion of the propensity score quintile. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

The baseline characteristics of TRT users and nonusers are presented in Table 1. Patients who were not in the propensity score overlap region were removed, reducing the final hypogonadal men cohort to 1,290 patients including 240 TRT user patients and 1,050 TRT non-user patients. Table 2 presents the results of the multivariable logistic regression analyses. After adjusting for demographic, clinical and health services covariates, TRT was not associated with a decreased 30-day rehospitalization following PAC (OR=0.87, 95% CI, 0.59-1.29). These findings persisted after adjustment for quintile of propensity score analyses (OR=0.90, 95%CI=0.62-1.30).

DISCUSSION

In this nationally representative cohort study of testosterone deficient older men, the use of TRT was not associated with lower 30-day hospital readmission following post-acute care after adjustment for multiple demographic, clinical, and health services variables, and across several propensity score approaches. To our knowledge, this is the first study to examine this relationship.

Discharges of clinically unstable patients to PAC facilities have increased due to Medicare's change to a prospective payment system for hospitals in the 1980s coupled with the rise of managed care in the 1990s.² Rehospitalization from PAC facilities occur early in functionally disabled older patients who would need more intensive health care. Overall, 22.2% of readmissions from PAC facilities occurred more than 30 days after hospital discharge and functionally disabled patients, with markers of higher acuity—defined as

more hospitalizations in the 6 months prior to the index hospitalization, a longer hospital length of stay before PAC facility transfer, more physician visits in the PAC facility, need for intravenous medications, and heart failure as the primary diagnosis— were more likely to be readmitted. Readmitted patients were twice as likely as non-readmitted patients to die in the 30 days following hospital discharge and nearly four times as likely to die in the 100 days post-hospital discharge.²

Lengthy hospitalization can have adverse effects on the physical health and independence of older adults. Immobilization and long hospital stays can accelerate loss of lean body mass, sarcopenia, and mortality in older adults.^{21,22} These effects could be exacerbated in older men with hypogonadism, given that testosterone deficiency is independently associated with sarcopenia and overall functional health decline.¹¹

Positive effects of TRT on maintaining lean tissue mass and bone structure are well documented in older men with hypogonadism.¹²⁻¹⁴ Observational studies suggest benefits of TRT for hypogonadal men with osteoporotic fractures and frailty.²³⁻²⁵ These positive effects can persist for 6 months after cessation of the hormonal intervention.²⁶ Moreover, the Endocrine Society recommends the use of TRT in men with symptomatic low testosterone levels who are at high risk of bone fractures.²⁷

Given the chronicity of hypogonadism and its treatment, it will be important for future studies to examine of effects and benefits of TRT over long period of time. Such studies— especially those that assess functional independence and total health care utilization and associated costs—will have broad clinical and public health relevance.

Our study has several limitations. First, outcomes and risk factors information came from diagnosis codes included in outpatient and hospitalization services charges and such diagnoses are not always accurate or complete.²⁸ Second, given the observational nature of our study, it is likely that our findings have been affected by undetected selection bias. For example, older men on TRT may have been more likely than their peers to have engaged in positive health behaviors (e.g., healthy diet, exercise). Alternatively, testosterone deficient men who use TRT may have had more severe form of hypogonadism than those who did not use TRT. The latter scenario could have biased our findings in the direction of the null hypothesis. Additionally, we couldn't gather information on several important health behaviors such as smoking status, exercise, and diet. In this regard, it is somewhat reassuring that the addition of measured potential confounders had little effect on the association of TRT with PAC readmission. Furthermore, it is possible that some men may have chosen to seek treatment outside their usual health care setting, such as specialty hormone clinics driven by the perceived social stigma associated with receiving TRT. We did not have access to laboratory data, and therefore were not able to assess whether prescription of TRT resulted in normalization of low testosterone levels. It is possible that some TRT-treated patients continued to experience hypogonadism after discharge. Such insufficient TRT adherence or dosing would have likely biased our findings toward the null hypothesis. Despite these limitations, we believe this study has important strengths including a cohort that is representative of all US geographic regions and is inclusive of a socioeconomically diverse cohort.

Overall, our study suggests that TRT is not associated with reduced 30 days rehospitalization following PAC discharge in older men with testosterone deficiency. Further research in this population should examine the effects of TRT on functional recovery and other outcomes associated with functional health, such as community independence, risk for long-term care, and overall quality of life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations and Acronyms:

PAC	post-acute-care
TRT	testosterone replacement therapy
OR	odds ratio
CI	confidence interval
ICD-9-CM	International Classification of Diseases, ninth revision, clinical modification

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Table 1.

Baseline Demographic and Clinical Characteristics for Testosterone Users and Nonusers

Characteristic ^a	TRT <i>n</i> (%) or mean (st.dev)	No TRT <i>n</i> (%) or mean (st.dev)	<i>P</i> -value	
			Before PS adjustment ^b	After PS Adjustment ^b
All	240 (100)	1,050 (100)		
Age (years) at index PAC stay (Mean)	75.7 (6.3)	78.1 (7.2)	<i>P</i> <.001	<i>P</i> =.22
Age (years) at index PAC stay				
66-69	53 (22.1)	163 (15.5)		
70-74	65 (27.1)	229 (21.8)		
75-79	61 (25.4)	246 (23.4)		
80	61 (25.4)	412 (39.2)	<i>P</i> <.001	<i>P</i> =.71
Race				
White	219 (91.3)	890 (84.8)		
Black	9 (3.8)	65 (6.2)		
Hispanic	9 (3.8)	68 (6.5)		
Other	3 (1.3)	27 (2.6)	<i>P</i> =.08	<i>P</i> =.89
Education (% high school education) ^c				
Q1:	52 (21.7)	274 (26.1)		
Q2:	55 (22.9)	267 (25.4)		
Q3:	72 (30)	269 (25.6)		
Q4:	61 (25.4)	240 (22.9)	<i>P</i> =.26	<i>P</i> =.76
Household Income ^d				
Q1:	60 (25.0)	270 (25.7)		
Q2:	62 (25.8)	259 (24.7)		
Q3:	58 (24.2)	256 (24.4)		
Q4:	59 (24.6)	263 (25.1)		
Unknown	1 (0.4)	2 (0.2)	<i>P</i> =.96	<i>P</i> =.95
Duration of index IRF/SNF stay (days)			<i>P</i> =.02	<i>P</i> =.03
1-8	25 (10.4)	217 (20.7)		
9-13	56 (23.3)	226 (21.5)		
14-20	47 (19.6)	203 (19.3)		
21-34	51 (21.3)	195 (18.6)		
35	61 (25.4)	209 (19.9)		
Hospitalization during the preceding 12 months			<i>P</i> =.24	<i>P</i> =.80
0	6 (2.5)	31 (3.0)		
1	133 (55.4)	521 (49.6)		
2	59 (24.6)	255 (24.3)		
3	42 (17.5)	243 (23.1)		
Outpatient visits during the preceding 12 months			<i>P</i> =.005	<i>P</i> =.68
0-7	66 (27.5)	221 (21.1)		

Characteristic ^a	TRT <i>n</i> (%) or mean (st.dev)	No TRT <i>n</i> (%) or mean (st.dev)	<i>P</i> -value	
			Before PS ^b adjustment	After PS ^b Adjustment
8-13	57 (23.8)	198 (18.9)	<i>P</i> =.12	<i>P</i> =.84
14-18	48 (20.0)	251 (23.9)		
19-25	38 (15.8)	184 (17.5)		
26	31 (12.9)	196 (18.7)		
Elixhauser Comorbidity score				
0-3	60 (25.0)	230 (21.9)		
4	44 (18.3)	136 (13.0)		
5-6	56 (23.3)	272 (25.9)		
7-8	44 (18.3)	232 (22.1)		
9	36 (15.0)	180 (17.1)		

^a All percentages and frequencies are unadjusted

^b PS= propensity score

^c Percentage of persons (aged ≥ 25 years) in zip code with at least a high school education, presented by quartile

^d Median household income in zip code, presented by quartile

Table 2.

Odds Ratios (ORs) rehospitalization outcome associated with TRT

Analytic Method	All 30-day PAC Readmissions OR (95% CI)
Unadjusted	0.81 (0.57, 1.17)
Adjusted for all covariates	0.87 (0.59, 1.29)
Adjusted for quintile of propensity score	0.90 (0.62, 1.30)