

SH5: Should testosterone supplementation be stopped prior to and for a period of time after arthroplasty? If so, when should it be restarted.

Liaison: Benjamin Zmistowski

Lead delegate: Usama Hassan Saleh

Supportive delegates: Ahmed Saeed Younis, Helmi Abdalbari

Supportive authors: Alfonso Ayala (Uni Nevada)

Response: There is not sufficient data to currently support withholding testosterone replacement therapy (TRT) prior to shoulder arthroplasty. There is no data providing guidance on timing of TRT cessation prior to shoulder arthroplasty.

Level of recommendations: Limited

Delegate Vote: 50 (98%) agree; 0 disagree; 1 (2%) abstain

Rationale: Periprosthetic joint infection (PJI) is a rare, but serious, complication following primary shoulder arthroplasty with an incidence ranging from 1 to 2.1 % [1][2][3]. Male gender and younger age are key risk factors for periprosthetic shoulder arthroplasty[3]. Testosterone replacement therapy (TRT) is commonly used to treat hypogonadism in aging males[4][5]. Studies suggest that TRT increases serum testosterone levels and *C. acnes* skin colonization[6], a bacterium frequently implicated in the development of periprosthetic shoulder infection.[7] However, the direct link between TRT, altered skin bacterial colonization, and increased PJI risk remains under investigation.

We conducted a literature search in PubMed and Scopus databases and we found six studies for inclusion. Matsen et al. 2020 have investigated the microbiology and bacterial colonization of the epidermal surfaces of patients undergoing primary shoulder arthroplasty. They found that *C. acnes* was the most prevalent organism in skin flora of these patients. Also they found that male patients on testosterone supplements are more likely to have greater colonization with *C. Acnes* in the incised dermis for a primary shoulder arthroplasty. The risk of PJI may also increases with male sex hormones and high testosterone level which alter the biology of the skin sebaceous glands, hair follicles and increase *C. acnes* colonization [8]. Frederick et al. 2020 in another retrospective review of 342 patients undergone prosthetic shoulder revisions after primary shoulder arthroplasties. They found that there was higher *C. Acnes* revisions in young male patients with higher prevalence of testosterone supplementation in those patients [9]. Siffman et al. 2021 studied the relationship between testosterone level and preoperative *C. Acnes* skin colonization. They measured the free testosterone level and total serum testosterone and sex hormone binding globulin levels and related it in a multivariate analysis to *C. Acnes* colonization in clinic and preoperative skin cultures. They found high rate of *C. Acnes* colonization in patients with high blood testosterone level[6]. A major limitation of these studies is the high rate of culturing contamination and different culturing methods. Favian et al. 2023 is a retrospective cohort study that compared a cohort receiving testosterone supplement (2285 patients) to a control group not receiving TRT

(4172 patients) who underwent primary shoulder arthroplasty. They found that use within 6 months of shoulder arthroplasty may be associated with higher rates of prosthesis joint infection. However, patients who were taking testosterone but stopped before surgery did not have a higher rate of infection compared to those who never used the medication[10]. Coden et al. 2024 retrospectively reviewed the effect of testosterone replacement therapy on reoperation rate after total shoulder arthroplasty. They found a higher reoperation rate due to infection after 2 years of TRT supplementation (2% of 448 patients) compared to non TRT receivers (0.9% of 2240 patients) [11]. Parmar et al. compared the outcomes of reversed total shoulder arthroplasty between two groups either receiving TRT therapy or not. The TRT group included 1906 patients receiving testosterone therapy mainly for causes of hypogonadism, erectile dysfunction, decreased libido, and benign prostatic hyperplasia. They found no increased risk of revision or PJI in this group compared to a comparable group (1906 patients) not on TRT therapy [12]. The clinical studies investigating the relation between testosterone supplementation and the risk of shoulder PJI are very few and have many limitations. These clinical studies are retrospective comparisons of unmatched cohorts and their conclusions are contradicting and of limited evidence. Although most of the included studies identify high rates of *C. Acnes* skin colonization in patients receiving testosterone supplementation which is the most common isolated organism from shoulder PJI cultures, these data are weakly supported by clinical reports. Conversely, young males on testosterone supplementation who are seeking the improvement of their general health and physical performance are the most likely to benefit from shoulder arthroplasty surgery. So further clinical studies are needed to investigate the relation between testosterone supplementation and PJI, recommending stoppage of such treatment before arthroplasty or even marking those patients as high risk of PJI.

High levels of serum testosterone may be a risk factor of high *C. Acnes* skin colonization which is a risk factor for shoulder PJI. However, there is insufficient clinical data to support this evidence. The only studied timepoint for stopping testosterone use was 6 months, showing no difference in infection risk in patients on testosterone supplementation > 6 months. There is no guidance on when it is safe to restart testosterone replacement therapy. Further studies are needed to find the exact relation between testosterone supplementation and shoulder PJI and any necessary stopping time.

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