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Authors
Andino, Juan J
Mills, Jesse N

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EDITORIAL COMMENTS

We commend the authors for the immense effort of completing a randomized controlled trial with the 2 guideline-recommended treatment options for Peyronie's disease: Food and Drug Administration–approved collagenase *Clostridium histolyticum* (CCH) injections and surgery (including penile plication and/or incision and grafting).[1]

The authors ensured that the data would be relevant to modern-day practice by incorporating the use of a standardized protocol of the RestoreX penile traction device as well as daily sildenafil to facilitate the comparison of outcomes between the treatment groups.

This randomized trial is consistent with the real-world experience at our institution, where patients who do not have extreme curvatures or deformities tend to choose a round of CCH prior to considering penile surgery.[2] Importantly, surgical outcomes for patients who do not respond sufficiently to injections are not negatively impacted by prior CCH treatments. As our field advances, the indications for CCH treatments will continue to broaden when supported by rigorous research. For instance, men with ventral curvature and those with persistent, distinct plaques can benefit from additional rounds of CCH if not willing to proceed with surgery.[3] Similarly, Masterson et al demonstrated that calcified plaques show similar treatment response to CCH compared to noncalcified plaques, potentially expanding future treatment options as insurance coverage can sometimes dictate the decision for patients.[4]

We look forward to the follow-up studies with long-term outcomes. The data from this randomized controlled trial will further facilitate patient counseling, as CCH injection techniques and surgical approaches continue to evolve. Is eliminating the curvature as fast as possible the priority? What about reducing the risk of complications such as worsening erectile dysfunction or sensory changes? At the end of the day, it is the penis and the deformity caused by the disease process that should drive the shared decision-making process—informed by the patient's preference and the surgeon's experience.

Juan J. Andino[1] and Jesse N. Mills[1]
[1]*Department of Urology*
University of California, Los Angeles
Santa Monica, California

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Green and colleagues report the results of a randomized controlled trial comparing collagenase *Clostridium histolyticum* (CCH) + RestoreX penile traction device + sildenafil to surgery + RestoreX + sildenafil.[1] The authors should be congratulated on completing a very well-designed study as it is quite remarkable to complete a study randomizing men to surgery vs an alternative intervention. At 3-month follow-up, they found a higher subjective erectile function, less change to penile sensation, and less change to penile length in men undergoing CCH + RestoreX + sildenafil. Their results provide a great addition to the Peyronie's disease (PD) literature which can help aid surgeons when counseling patients.

Although it was not statistically significant, overall satisfaction was higher (50% vs 21%, $P = .08$) in the CCH group despite the surgery group having a statistically greater curve improvement (65° vs 32.5°, $P = .02$). Many physicians who treat PD feel if you improve the curvature it should translate to patient satisfaction. The results of this randomized study suggest patient satisfaction is a more complex issue than just curvature correction. This study found more adverse events in the surgery group which may be a major contributor to patient satisfaction. It should be noted that length loss was considered an adverse event. Almost all (18/19) of the surgery patients underwent penile plication, and some surgeons would not consider length loss an adverse

event, but rather an expected outcome and one that may lead to less satisfaction even after extensive counseling from very experienced PD surgeons.

The follow-up period for this publication was only 3 months. Although it is a short period of time, most adverse events should be captured; however, satisfaction may change more over time. We commend the authors on a well-designed and -executed study, and eagerly await the 1- and 5-year data.

David W. Barham[1] and Faysal A. Yafi[1]
[1]*Department of Urology*
University of California, Irvine
Orange, California

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Despite the advent of the first Food and Drug Administration–approved intralesional injection therapy, collagenase *Clostridium histolyticum* (CCH), surgery maintains its position as the gold standard treatment for men seeking to restore their penis to its pre-Peyronie's disease appearance. The study at hand randomized men with >30° of curvature to either CCH or surgical penile straightening, with plication or incision/grafting.[1] All participants used traction therapy (RestoreX) and sildenafil.

Statistically significant differences were observed: subjective erectile function, penile length, and the impact on penile sensation all favored CCH, while surgical intervention showed greater improvements in curvature. However, surgery was associated with increased rates of penile pain, loss of length, palpable lumps, and sensory changes.

The authors of this study deserve recognition for their well-conducted, though somewhat small, randomized trial. Their comparison of various patient-reported outcomes and objective measures between surgical and medical treatment makes a meaningful contribution to the literature. That said, it is important to bear in mind that the results might inherently reflect the authors' extensive familiarity and expertise with CCH injection. Thus, clinics with lower volumes or different approaches may not yield similar results.

The relatively brief follow-up duration may also introduce bias against surgical interventions, given that symptoms such as pain, swelling, palpability, and sensory changes tend to improve up to 1 year postoperatively. Considering that the majority of surgical straightenings in the study involved plication rather than grafting, it is not surprising that length loss was more prevalent in the surgical group. Certain technical aspects, like graft choice in the few grafting cases, may have likewise impacted surgical outcomes.

When addressing Peyronie's disease, it's clear that no single solution fits all scenarios, demanding an individualized treatment approach. This study aids in discussing the merits of CCH vs plication, while also reinforcing the need for further investigation, ideally with longer-term follow-up.

Bradley J. Roth[1] and Petar Bajic[1]
[1]*Center for Men's Health*
Glickman Urological and Kidney Institute
Cleveland Clinic
Cleveland, Ohio

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REPLY BY AUTHORS

We greatly appreciate the comments by our colleagues. The current study reveals several interesting findings about Peyronie's disease and its treatment.[1] First, satisfaction appears to be driven by adverse events as much as outcomes. Although we may wish to achieve surgical perfection, the data would suggest that patients are more interested in not making things worse at the expense of improvements.

Second, although both groups desired collagenase *Clostridium histolyticum* initially, posttreatment

each arm preferred the therapy they received. This finding helps explain the large discrepancy in the literature which demonstrates low rates of Peyronie's disease men choosing surgery, while at the same time reporting satisfaction after the fact.[2]

Third, Surgery men did not report greater improvements in indentation/hourglass deformities despite undergoing procedures designed to address those issues. Although this is usually an argument in favor of surgery, it is not supportable with the current data.

Fourth, the current study represented an all-comer population, including severe curvatures, hourglass deformities, ventral direction, and calcifications. Overall results validated our prior series, wherein improvements were noted in ventral men and linearly correlated with calcification (none/mild = 36° improvement; moderate/severe = 20°).[3,4] Of note, these findings (and our prior series) contrast to the Masterson report which may relate to differing classification schemes.[5]

Finally, the current study was not designed (powered) to demonstrate superiority of one therapy over another. However, it clearly shows that collagenase *C histolyticum* would not be considered an inferior treatment, regardless of disease severity, and may be considered an equivalent gold standard when administered using optimal protocols.

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