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European Association of Urology

Brief Correspondence

Dehydrated Human Amnion/Chorion Membrane Allograft Nerve Wrap Around the Prostatic Neurovascular Bundle Accelerates Early Return to Continence and Potency Following Robot-assisted Radical Prostatectomy: Propensity Score–matched Analysis

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Article info

Article history:
Accepted January 13, 2015

Keywords:
Biological dressings
Prostatic neoplasms
Robotics
Erectile dysfunction
Urinary incontinence
Convalescence

Abstract

We present a propensity-matched analysis of patients undergoing placement of dehydrated human amnion/chorion membrane (dHACM) around the neurovascular bundle (NVB) during nerve-sparing (NS) robot-assisted laparoscopic prostatectomy (RARP). From March 2013 to July 2014, 58 patients who were preoperatively potent (Sexual Health Inventory for Men [SHIM] score >19) and continent (no pads) underwent full NS RARP. Postoperative outcomes were analyzed between propensity-matched graft and no-graft groups, including time to return to continence, potency, and biochemical recurrence. dHACM use was not associated with increased operative time or blood loss or negative oncologic outcomes ($p > 0.500$). Continence at 8 wk returned in 81.0% of the dHACM group and 74.1% of the no-dHACM group ($p = 0.373$). Mean time to continence was enhanced in group 1 patients (1.21 mo) versus (1.83 mo; $p = 0.033$). Potency at 8 wk returned in 65.5% of the dHACM patients and 51.7% of the no-dHACM group ($p = 0.132$). Mean time to potency was enhanced in group 1, (1.34 mo), compared to group 2 (3.39 mo; $p = 0.007$). Graft placement enhanced mean time to continence and potency. Postoperative SHIM scores were higher in the dHACM group at maximal follow-up (mean score 16.2 vs 9.1). dHACM allograft use appears to hasten the early return of continence and potency in patients following RARP.

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Over the last two decades there has been improvement in our understanding of prostatic anatomy and the surgical technique of radical prostatectomy. Robot-assisted radical prostatectomy (RARP) has brought about advantages such as enhanced 10× magnification, three-dimensional vision, and the dexterity of miniaturized instrumentation. However, even for patients with well-preserved neurovascular bundles (NVBs) there remains a convalescent period characterized by incontinence and impotence [1]. This delay is probably due to an inflammatory response caused by traction injury to the NVB [2].

Physical traction on the NVB can be minimized by the surgeon but cannot be eliminated during mobilization of the prostate [3]. Tewari et al [3] used a traction monitor to evaluate the aspects of RARP inflicting the greatest mechanical force and showed that reduced NVB traction diminishes

http://dx.doi.org/10.1016/j.eururo.2015.01.012
0302-2838/

ischemic nerve injury. Finley et al [4] tested regional hypothermia via a rectally placed cooling balloon. The group demonstrated improvements in the return of urinary continence, but not early sexual function. We have been awaiting the next step in innovation that transcends the technical aspect of nerve-sparing (NS) by biologically altering the prostatic NVB neuropraxia induced by surgical dissection [3]. Clinical use of growth factors and anti-inflammatory substances for prostatic NVB regeneration is novel, and dehydrated human amnion/chorion membrane (dHACM) is a source of implantable neurotrophic factors and cytokines [5,6]. The aim of our feasibility study was to ascertain if any functional benefit could be measured after placement of dHACM around the NVB following full NS RARP.

Full institutional board approval was granted for this study. Patients were included from the period March 2013 to July 2014 at our institution. All RARP procedures were performed by a single surgeon using the transperitoneal six-port technique with a Da Vinci surgical system (Intuitive Surgical, Sunnyvale, CA, USA). Bilateral, retrograde, athermal NS RARP was performed in each patient, with bladder neck reconstruction, an anterior suspension stitch, and posterior reconstruction (Rocco stitch). There were 58 patients in this series, who were preoperatively continent (American Urological Association Symptom Score <10) and potent (Sexual Health Inventory for Men [SHIM] score >19) and underwent bilateral dHACM placement (AmnioFix; MiMedx Group, Marietta, GA, USA) at a cost of $900 per patient (Supplementary Fig. 1). The dHACM allograft was cut into two longitudinal pieces and placed over each NVB as a nerve wrap. The wrap was placed circumferentially around the NVB after extirpative RARP, post anastomosis. The dHACM study cohort (group 1; $n = 58$) was computer-matched with a similar group of patients

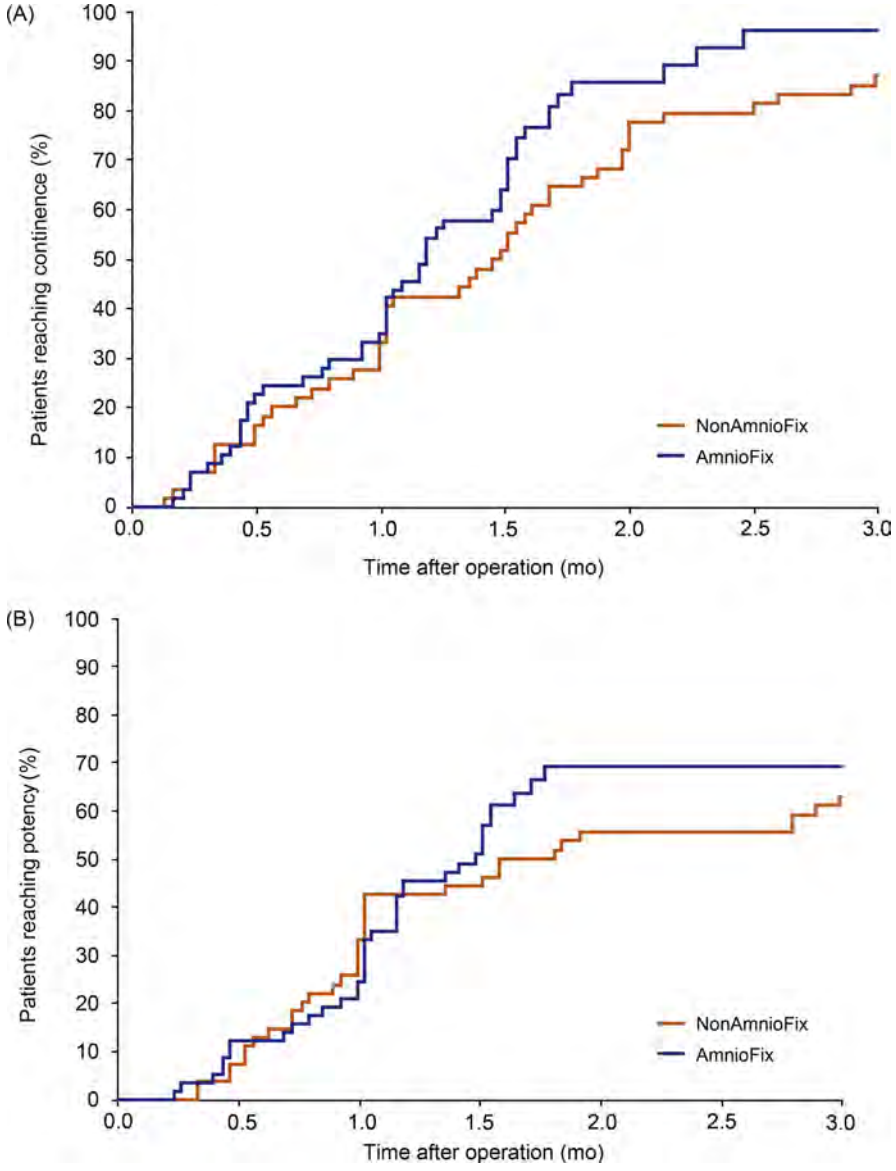

Fig. 1 – Cumulative index curves showing (A) time to continence and (B) time to potency. Time to reach continence: AmnioFix group, 1.21 mo; nonAmnioFix group, 1.83 mo ($p = 0.033$). Time to reach potency: AmnioFix group, 1.34 mo; nonAmnioFix group, 3.39 mo ($p = 0.007$).

who did not receive a dHACM graft (group 2; $n = 58$) in a multivariate design to create homogeneous groups.

Follow-up information was obtained through comprehensive questionnaires and clinic or telephone interviews. Postoperative continence was defined as use of no pads per day. Potency was reported by patients as the ability to achieve and maintain an erection with or without a phosphodiesterase type 5 inhibitor. A description of the statistical analyses performed is provided in the Supplementary methods. There were no significant preoperative differences between the groups (Supplementary Table 1). Intraoperative parameters were comparable between the groups (Supplementary Table 2), with no postoperative morbidity in either group (Supplementary Table 3).

The minimum 8-wk follow-up was complete for all patients in both groups, with an average follow-up of 4 mo. Continence at 8 wks returned in 81.0% of patients in group 1 and 74.1% of patients in group 2 ($p = 0.373$). The mean time to continence was shorter in group 1 (1.21 mo) than in group 2 (1.83 mo; $p = 0.033$, Fig. 1A). Potency at 8 wk returned in 65.5% of group 1 patients and 51.7% of group 2 patients. The mean time to potency was significantly shorter in group 1 (1.34 mo) than in group 2 (3.39 mo; $p = 0.007$, Fig. 1B). SHIM scores were also higher for group 1 than for group 2 (mean score 16.2 vs 9.1).

We evaluated all patients at their first postoperative visit at 8 wk. Our results indicate that dHACM placement facilitates early return to continence and potency. The mean times to potency and continence were significantly shorter in the allograft group. dHACM facilitates wound healing and has been used to treat burns, corneal injuries, chronic venous ulcers, and chronic wounds [7]. Neurotrophic factors present in dHACM promote nerve cell survival and maintain target organ function by facilitating axon regeneration [8]. A number of recent experimental studies using neurotrophic growth factors and dHACM have provided encouraging data regarding the potential to rehabilitate nerves after injury (Supplementary references). The bilayered amnion and chorion membrane graft we used has nonviable cells and an array of growth factors (Supplementary Fig. 1).

Our data are encouraging for the study of anti-inflammatory agents at the site of the prostatic NVB. However, our study has several limitations; it is an observational study with retrospective data collection and is subject to patient recall bias. The lack of prospective randomization is compensated by our large patient pool available for propensity matching, and our optimal matching algorithm ensured there were no significant preoperative differences between the comparison groups (Supplementary Table 1). Long-term oncologic results are being recorded, and longer follow-up is required to evaluate future outcomes for our cohort.

Following RARP, the degree of NVB preservation is correlated to improved recovery of urinary continence and potency [9], suggesting that preservation of neural tissue is associated with enhanced functional outcomes, while the NS mode (retrograde vs antegrade) has no impact on margin status [10]. In this study, dHACM accelerated the return of continence and potency in patients following NS RARP, with no adverse effects (Supplementary Table 4). An adequately powered, prospective randomized trial and cost-benefit analysis of dHACM around the prostatic NVB are now under way to further ascertain the treatment effect of this new approach. In conclusion, our short-term results are encouraging for patients undergoing full NS RARP and dHACM placement.

Author contributions: Vipul R. Patel had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Patel, Samavedi, Bates.
Acquisition of data: Patel, Samavedi, Bates, Kumar, Coelho, Rocco, Palmer.
Analysis and interpretation of data: Patel, Samavedi, Bates, Kumar, Coelho, Rocco, Palmer.
Drafting of the manuscript: Patel, Samavedi, Bates, Kumar, Coelho, Rocco, Palmer.
Critical revision of the manuscript for important intellectual content: Patel, Samavedi, Bates, Kumar, Coelho, Rocco, Palmer.
Statistical analysis: Patel, Samavedi, Bates, Kumar, Coelho, Rocco, Palmer.
Obtaining funding: Patel, Samavedi, Bates, Kumar, Coelho, Rocco, Palmer.
Administrative, technical, or material support: Patel, Samavedi, Bates, Kumar, Coelho, Rocco, Palmer.
Supervision: Patel, Samavedi.
Other: None.

Financial disclosures: Vipul R. Patel certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: Vipul R. Patel is a consultant for MiMedx.

Funding/Support and role of the sponsor: None.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.eururo.2015.01.012.

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