Editorial

Complications after salvage radical prostatectomy: vesicourethral anastomosis leaks and possible prevention

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Comment on: Ogaya-Pinies G, Kadakia Y, Palayapalayam-Ganapathi H, *et al*. Use of Scaffolding Tissue Biografts To Bolster Vesicourethral Anastomosis During Salvage Robot-assisted Prostatectomy Reduces Leak Rates and Catheter Times. Eur Urol 2016. [Epub ahead of print].

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Next to radical prostatectomy (RP), definitive radiotherapy (RT) represents one of the most common treatment modalities for localized prostate cancer (PCa). Yet, 22%–63% of RT patients will develop biochemical recurrence (BCR) after primary treatment (1,2). While RT is considered a valid second line option after surgical failure, the majority of radiation-recurrent patients will receive androgen deprivation therapy (ADT) (1,2). However, in the setting of local recurrence, standard management with ADT might result in overtreatment without curative intent that causes several life-lasting side effects and harms Quality of life (QoL) (3). In consequence, more tailored options that balance the relation of cancer control while optimizing QoL and reducing lasting side effects are needed. In this context, the role of salvage radical prostatectomy (SRP) has evolved over the last decade. A recent review by Chade *et al*. demonstrated safety and improvement of different outcomes after SRP (4). Their review included publications on SRP between 1980 and 2011 and analyzed the trend over time for complications, pathological, oncological and functional results. The authors revealed improved pathological outcomes showing for example decreased rates of positive surgical margins (PSM) ranging from 43–70% in earlier to 0–36% in more recent reports. Similarly, more recent reports showed higher rates of organ-confined disease compared to earlier series (44–73% *vs*. 22–53%). Moreover, the authors postulated durable oncological outcomes with 5- and 10-year biochemical recurrence-free survival (BFS) rates ranging between 47–82% and 28–53% (4). Most recently, Marra *et al*. presented pathological and oncological outcomes among 243 SRP patients in a multicenter setting. Here, the authors found PSM in 37% and extra-prostatic extension in 49% of the patients. During the follow-up period (median 37 months), 44% developed BCR (5).

To improve cancer control, patient selection for SRP is essential. In this context, Mandel *et al*. showed considerably higher BFS rates in SRP patients that met the EAU guideline criteria for SRP (6). The study included 55 SRP-patients, 32 who met *vs*. 23 who did not meet EAU criteria and reported 5-year BFS rates of 73.9% *vs*. 11.6%.

Nevertheless, SRP remains a challenging procedure that can lead to severe complications (4). Due to radiation induced tissue adhesions and vessel injuries, rectal lesions and hemorrhages are the surgeon's major concerns (4,7). One other frequently observed complication is an anastomotic leak after vesicourethral anastomosis (VUA) (8,9). The subsequent urine leakage results in longer catheterization and might predispose to urethral strictures and bladder neck contractures (10). Although the latter relation has not been conclusively investigated, several authors support the theory that anastomic leaks may lead to persistent inflammatory which in consequence can restrict the wound healing process and subsequently cause contractures or stenosis (10).

Traditionally, SRP was performed using an open surgical

technique. In 2008, Jamal *et al*. were the first, that reported a single case of salvage robotic assisted laparoscopic RP (sRALP) in a 50-year-old man with radiation-recurrent PCa (11). Up to date, only few smaller series added information on feasibility and safety in the context of sRALP (8,12-14).

One of the largest series on sRALP was published in 2014 by Yuh *et al*. In their report, the authors retrospectively analyzed 51 patients that underwent sRALP between 2004 and 2012 and found anastomic leaks in 18% of patients (8). All patients underwent cystography two weeks after sRALP. In case of urine leakage, the transurethral catheter was left in situ for another week. Median catheterization time was 15 days and in two cases following bladder neck contracture was attributed to the anastomic leaks. With 34%, Bates *et al*. observed an even higher rate of anastomic leaks in 53 patients undergoing sRALP compared to 53 primary RALP controls between 2008 and 2014 (12). Cystographic urinary leakage was found in 18 (34%) sRALP patients compared to three (6%) primary RALP patients. No information on urethral strictures or bladder neck contractures was available in their series. Similarly, Eandi *et al*. reported on 18 sRALP patients between 2004 and 2008 (9). Cystography was performed on day 10 to 14 and revealed anastomic leaks in six patients (33%). Overall, three (17%) urethral strictures were registered. All of them occurred in patients that had previous anastomic leaks. In consequence, novel techniques to improve VUA and prevent anastomic leaks are of high interest.

In an article for the Surgery in Motion section of European Urology, Ogaya-Pinies and colleagues described feasibility, safety and functional outcomes for the use of a scaffolding tissue graft to prevent VUA rupture after salvage RALP (15). In 15 sRALP patients, a single surgeon incorporated porcine urinary bladder extracellular matrix (UB-ECM) into the posterior part of the VUA base and distal bladder neck. To this aim, the UB-ECM scaffold was cut as a triangle with a rectangular piece attached to the base and placed with the tip facing the bladder neck and the rectangular part close to the urethra. In the next step, the scaffold was sutured to the Denonvilliers' fascia and after VUA, the rectangular part was wrapped around the anastomosis. These 15 procedures (group I) were 1:3:3 matched to 45 control sRALP without UB-ECM implantation (group II) and 45 primary RALP controls (group III). On day ten, all patients underwent control cystography. VUA rupture was defined as a contrast leak of >2 cm. Median follow-up was 12 months. The authors found radiologic disruption of the VUA in one of the patients in group I compared to 16 patients in group II and none in group III (P=0.0001). Accordingly, the median catheterization time differed between the three groups with 10.5 days in group I, 17.4 days in group II and 6.3 days in group III. However, 12-month urinary continence rates, defined as pad-free status, were similar among group I and II and significantly higher in group III (53% *vs*. 49% *vs*. 98%). During the follow-up, no major complications, bladder neck contractures or urethral strictures were reported among all 105 patients. The authors postulated that incorporation of an UB-ECM scaffold in the VUA is a promising method to reduce anastomic leaks. With this report the authors investigated an important problem after sRALP and presented an innovative technique. Although incorporation of the scaffold did not result in better long-term UC rates, the rate of anastomic leaks and catheterization time were significantly reduced. Especially longer catheterization may result in considerable patient discomfort and can cause several complications such as urinary tract infections (16,17). Furthermore, it is of note, that prolonged catheterization might be associated with worse short-term UC (18). For example, Palisaar *et al*. showed an adverse effect of prolonged catheterization (≤7 *vs*. 8–15 *vs*. >15 days) on six-week UC, defined as ≤1 pad/24 hours in 2998 patients who underwent open RP or RALP (18).

The used acellular ECM scaffold is derived from the basement membrane and lamina propria of porcine urinary bladder. By now, the underlying mechanisms for the constructive remodeling process that promotes differentiation to site-specific tissue are not completely understood. Despite induction of growth factors, degradation products of ECM are assumed to be responsible for subsequent recruitment and proliferation of suitable cell types (19).

As the authors stated, no previous studies examined ECM scaffold in the context of urologic surgery. However, utilization of ECM can be found in numerous preclinical and clinical applications such as wound management, corneal reconstructions or esophagojejunal anastomosis after gastrectomy showing promising results (20-22).

In summary, the authors provide a novel approach to solve the problem of anastomic leaks especially in the context of surgically challenging sRALP. Further studies, ideally in a randomized setting with higher patient numbers and more follow-up, are needed to verify these first results.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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