Tutolo, M., Cornu, J. N., Bauer, R. M., Ahyai, S., Bozzini, G., Heesakkers, J., ... Van Der Aa, F. (2018). Efficacy and safety of artificial urinary sphincter (AUS): results of a large multi-institutional cohort of patients with mid-term follow-up. *Neurourology and Urodynamics*. https://doi.org/10.1002/nau.23901

Peer reviewed version

Efficacy and safety of artificial urinary sphincter (AUS): results of a large multi-institutional cohort of patients with mid-term follow-up.

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43 Keywords: Artificial urinary sphincter, male stress urinary incontinence, surgical treatment

44 Word count abstract: 294

45 Word count text: 3216

46

47

48

ABSTRACT

AIMS: To assess efficacy and safety as well as predictive factors of dry rate and freedom from surgical revision in patients underwent AUS placement. The artificial urinary sphincter (AUS) is still considered the standard for the treatment of moderate to severe post-prostatectomy stress urinary incontinence (SUI). However, data reporting efficacy and safety from large series are lacking.

METHODS: A multicenter, retrospective study was conducted in 16 centers in Europe and USA. Only primary cases of AUS implantation in non-neurogenic SUI after prostate surgery, with a follow-up of at least one year were included. Efficacy data (continence rate, based on pad usage) and safety data (revision rate in case of infection and erosion, as well as atrophy or mechanical failure) were collected. Multivariable analyses were performed in order to investigate possible predictors of the aforementioned outcomes.

RESULTS: Eight hundred ninety-two men had primary AUS implantation. At 32 months mean follow-up overall dry rate and surgical revision were 58% and 30.7%, respectively. Logistic regression analysis showed that patients without previous incontinence surgery had a higher probability to be dry after AUS implantation (OR: 0.51, p=0.03). Moreover institutional case-load was positively associated with dry rate (OR: 1.18; p=0.005) and freedom from revision (OR: 1.51; p=0.00).

CONCLUSIONS: The results of this study showed that AUS is an effective option for the treatment of SUI after prostate surgery. Moreover previous incontinence surgery and low institutional case-load are negatively associated to efficacy and safety outcomes.

INTRODUCTION

The most common radical treatment for localized prostate cancer is radical prostatectomy (RP); however, major morbidities of this procedure includes stress urinary incontinence (SUI). Rates of postoperative SUI has been reported to range from 6% to 52%, most typically estimated as 6.3% - 19.3% [1]. Risk of SUI after transurethral treatment of benign prostatic obstruction has been estimated to be approximately 1% [2]

The European Association of Urology (EAU) Guidelines for Urinary Incontinence still considers AUS implantation the standard treatment for moderate-to-severe SUI in men [3]. This recommendation, however, is based on systematic reviews without high quality evidence (level 2b – 3), except for one small randomized clinical trial comparing AUS with bulking agents [4–6].

The most commonly used device is the AMS 800™ (Boston Scientific, Marlborough, MA, USA).

Based on retrospective and prospective single institution cohort studies, the AUS procedure has a high satisfaction rate (>80% over 4 years), which, however, is tempered by high revision rates (14-44% over 2 years) [7–20]. Indeed, only two prospective studies, accounting for 125 patients with a follow up of > 12 months, have been published [21–25]. Therefore, risk factors for efficacy or revisions rates remain uncertain. Moreover, only 17% of primary implants are performed by high volume centers (performing more than 10 implants per year) [22,26,27].

The aim of this study was to analyze the efficacy and safety of AUS in a large multi-institutional cohort of patients with medium term follow-up**.** We also performed a multivariable analysis to assess predictive factors of dry rate and freedom from surgical revision.

MATERIAL AND METHODS

Following an initiative from the Young Academic Urologists Working Party (YAUWP) of the EAU, a retrospective study was initiated. A common database of all cases of AUS implantations in men for non-neurogenic SUI following prostate surgery between 1989 and 2012 was established. A common template for data collection was created by the Functional Urology Group of the YAUWP and was sent out to all participating centres. No exclusion criteria regarding healthcare centres were applied. Only primary cases of AUS implantation in men for non-neurogenic SUI after prostate surgery, implanted via a perineal approach, with a follow-up of at least one year and with complete data on pad count and complications were included in the data collection phase. Pre-operative patient demographics and comorbidities as well as peri-operative data were collected. Post-operative data included events related to activation (success, delay or failure), early complication (reoperations and readmissions before activation), and follow-up data until last visit, including length of follow-up, SUI status (dry status, number of pads per day), number of revisions, complications (date and type). Data were collected by a single medical staff member per center, returning them anonymously to a single author that collected all data in a unique dataset, which was not further widespread. Data from the statistical analysis were shared between authors. FIG 1. At the end of data collection process, 931 cases were collected from 16 different institutions, and after review, 892 AUS patients, with at least 1 year follow up, were included in the final analysis (mean 56 per institution, median 38.5, range 15-266). Data on urodynamic examination were available for 450/892 (50,4%) of patients.

The main outcomes of the study were continence rate (based on pad usage) and complications (revisions and explantations). Social continence, defined as one pad or less/day, represents the most commonly used outcome in the AUS surgery literature. However, it has been criticized as even the use of one pad diminishes the quality of life perceived by the patient, and thus complete dryness may be the

most patient relevant outcome [28]. Therefore in our study, we defined efficacy as dry rate (DR): namely 0 pad/day. The rate of surgical revision (SR) was defined as the need for surgery due to recurrent incontinence or complications [25].

The following variables were studied as potential predictors for efficacy (dry rate) or freedom from surgical revision: age, presence of diabetes mellitus (DM), use of anticoagulation therapy, previous incontinence surgery (PIS), previous pelvic radiotherapy (RT), use of a double cuff, cuff size, institutional case load (ICL – total number of cases per center in the whole time lapse). Moreover **a** further sub-analyis on the association between the average number of cases per center per year and dry rate and freedom from surgical revision was performed.

We also evaluated the global complication rate (CR), including all cases of infection and erosion, as well as failure rate (FR), including all cases of urethral atrophy (typically presumed when SUI recurrence occurs during follow up with a functioning AUS) or mechanical failure (in any of the sphincter components, tubing or one of the connections). We evaluated the proportion of patients undergoing surgical revision for the aforementioned reasons.

Chi-square and Wilcoxon rank test were used to compare the TURP and RP groups. Kaplan–Meier analysis was used to estimate incontinence rates over time. The institution caseload for dry rate and surgical revision was modeled as natural log function and constant. Institutional case load was dichotomized according to the most informative cut-off predicting dry rate and revision rate. A caseload plateau was defined as an improvement in the outcomes <1% in the subsequent 50 procedures. Multivariable logistic regression analysis was used to identify the predictors of dry rate and freedom from surgical revision rate, and to assess the role of case-load on efficacy and safety outcomes. All analyses were performed using SPSS, IBM, Armonk,USA.

RESULTS

Descriptive characteristics of the cohorts are presented in Table 1. The majority of patients (85.9%) previously underwent RP and others (14.1%) underwent surgery for benign prostatic obstruction. Both groups were homogeneous in terms of age, previous incontinence surgery, RT, double cuff and cuff size. Mean follow up after primary AUS implantation was 32 months (median 20, range 12-300). Median patient age was 68 years (range 39-87). A significant statistical difference was observed in the use of anticoagulants and presence of DM (Table 1). Data on history of DM and anticoagulation therapy were available for all 892 patients. A history of DM was observed in 111/892 (12.4%) patients. At the moment of AUS implantation, 217/892 patients (24.4%) were taking anticoagulants or antiplatelet therapy. Data on preoperative antibiotics usage were available for 621/892 (69%), among them, preoperative prophylaxis was used in 181 patients (29%). Among the 168 patients (19%) who had undergone PIS, 75 had male sling implantation and 93 had peri-urethral balloons. Overall 257/892 (28.9%) patients also had adjuvant RT after prostatic surgery and prior to AUS implant; Among patients treated with TURP 30% had also RT. This can be explained by the fact that some patients treated with TURP were submitted to RT in case of prostate cancer incidental finding. Moreover some patients treated with RT for prostate cancer could have been treated subsequently with TURP for obstructive symptoms. A 4.5cm single cuff was implanted in 46.5% of patients, while 9.4% of patients were implanted with double cuff in 4 different centres.

Data on pre-operative number of pads were available for 547/892 patients (61.3%). At the time of surgery a total of 369/547 (67.2%) patients were using ≥5 pads/day (median 5, IQR 5-7), 20/547 (3.6%) used only 1 pad, 29/548 (5.3%) used 2 pads; 49/547 (8.9%) used 3 pads and 81 (14.8%) used 4 pads. Data on postoperative pad count were available for all patients.

Complications were reported in 248 (27.8%) patients: 60 patients (6.7%) had erosion, 38 (4.2%) infection, 32 (3.5%) were diagnosed with urethral atrophy and 118 (13.2%) with mechanical failure.

Overall dry rate and surgical revision were 58% and 30.6%, respectively. Figure 2 depicts the rate of incontinence over time. Of the 248 patients experiencing complications/failure, all but one (with mechanical failure) underwent surgical revision. The reason for revision was not available in 26/273 patients (9.5%).

Of 724 patients without PIS, 409 (57%) were dry, while of 168 with PIS, 80 (48%) achieved this goal after surgery and 88 (52%) did not. Among the 88 PIS wet patients, 27 had undergone male sling implant (30.6%) and 61 periurethral balloons (69.4%).

The best cut-off for dry rate and surgical revision was 39 and 42 respectively. Patients treated in centers with a ICL ≥ 39 resulted to achieve a significantly higher dry rate while patients treated in centers with a ICL ≥ 42 resulted to have significantly lower rates of surgical revision. Adjusted differences in dry rate and surgical revision according to institutional caseload are depicted in FIGURE (3 -4).

Multivariable logistic regression accounting for the aforementioned variables, namely: previous incontinence surgery, RT, double cuff implantation, cuff size, DM, anticoagulation therapy and ICL, showed that patients without PIS had a higher probability to be dry after AMS 800 implantation (OR: 0.51, p=0.03). Moreover ICL was positively associated with dry rate: higher volumes give higher continence rates (OR: 1.18; p=0.005). Other variables did not have statistically significant correlation with success (table 2). Institutional case load was the only variable statistically associated with freedom from surgical revision (OR: 1.51; p=0.00) (table 2).

In an additional analysis taking into account the average number of cases per institution per year, we showed that it positively correlates with dry rate (OR 1.05; p=0.005) and with freedom from surgical

revision (OR1.075, p=0.00), confirming the evidence that higher volumes give higher continence rates and lower surgical revision rates.

DISCUSSION

This is the first study to report mid-term outcomes following primary AUS implantation in a large, multinational cohort of patients with non-neurogenic SUI treated in both low and high volume centres with the last modification of the system (narrow back cuff). Most earlier publications have been single centre cohort studies from high volume centres including both primary AUS implants as well as revision cases [19]. At the moment we have data about baseline safety and efficacy of primary AUS implantation, but most of them come from smaller series. Furthermore, risk factors for AUS failure or complications are not well defined.

In our multinational study, after a minimum follow-up of 12 months, overall dry rate was 58%. The global revision rate was 31%. These results are in line with studies previously reported in the literature [19]. However, many different criteria have been used, without clear consensus about the definition of efficacy and safety after surgery. External comparison of outcomes with previously published studies is therefore difficult.

In our population, 29% of patients had undergone pelvic RT. Among them, 53% were considered dry, while 30% required surgical revision after AUS placement. The influence of RT on AUS implantation outcomes remains controversial. In a meta-analysis of 15 studies including 1886 patients, men with history of pelvic RT were at higher risk of surgical revision (risk ratio of 1.56, 95%CI 1.02–2.41 $p<0.05$, $I2 = 82.0\%$). The need for surgical revision was higher in the RP+RT population than in the RP patients (37.3%, 95%CI 23.4–51.1 vs. 19.8%, 95%CI 11.9–27.6; $p< 0.01$). Persistence of UI after AUS placement was higher in the RP+RT population than in the RP patients 29.5%, 95% CI 18.1–45.8 vs. 12.1% 95% CI 5.7–18.4 (p 0.003) [29]. In a retrospective analysis of AUS implants complicated by cuff erosion, Kaufman et al. evidenced a negative relationship between history of RT and device survival (mean device survival in RT patients 1.00 years 95% CI 0.36-3.00 vs 3.15 years 95% CI 1.95-

5.80) [30]. These findings are in contrast with our results. Differences in radiation doses, field delineation, radiation technology, could account for some of the observed variability. A recent retrospective study on 1632 men implanted with AUS, of whom 274 had a history of RT, evidenced that RT does not influence re-implantation-free and revision/removal-free survival (log rank test p=0.37 vs 0.052) [31], confirming our results.

Our analysis shows that PIS has a negative impact on dry rate (p=0.03), but not on freedom from surgical revision (p=0.30). In particular patient with previous incontinence surgery have a dry rate rate that is roughly 10% lower compared to the counterpart (48% vs. 57%). Therefore, when planning less invasive surgery (i.e. slings or balloons) the patient should be informed about the possible lower efficacy after a secondary AUS placement. On the other hand, the revision rates in this group are reassuring. Even in case of previous surgery, the risk of surgical revision, due to complication or failure, does not increase. In a small prospective case series assessing clinical results of AUS placement after failure of male sling surgery, mid-term results evidenced that results of this procedure are comparable to first-line AUS implantation in terms of continence (87%) and complications (17%) [32]. In a case series of 61 men after a failed primary male sling procedure, continence was higher with placement of an AUS, rather than by a secondary sling procedure (treatment failure of 6% and 55% respectively) [33].

We demonstrated that institutional caseload is associated to dry rate and surgical revision. A median ICL above 39 and 42 is a protective factor in terms of dry rate and surgical revision respectively. Moreover, we demonstrated that 150 cases are required to reach a plateau for both outcomes. Even though it is true that “practice makes perfect,” only an improvement <1% was observed in the subsequent 50 cases. According to these data, patients treated in high volume centers are more likely to

be dry and free from revisions and, in experienced hands (surgeons above 150 procedures), the outcome does not change appreciably.

In a single-center, single-surgeon, continuous series of implants, Lai et al. demonstrated that the number of complications and reoperations decreases after having performed the first 25 procedures in his experience (12 complications in the first 25 procedures vs. 3 in the following 25, relative risk 4.0, p= 0.012; 11 vs. 3 reoperations, relative risk 3.7, p 0.026)[34]. Another study showed that the learning curve for AUS placement has no plateau, with reduction of revisions even after 200 procedures: the risk of revision within 5 years from implant was estimated at 24% after the first 5 procedures, 18% after 100 procedures and 13% after 200 procedures. The same study also showed that the majority of patients are treated in smaller volume centres: two-thirds of patients were operated by surgeons with an experience of less than 25 AUS implants, and only 9% of patients were operated by highly experienced surgeons having performed more than 100 AUS implants [35].

Our results suggest that neither the presence of a double cuff nor cuff size influence the two main outcomes: dry rate and freedom from surgical revision. The choice of the cuff size is mainly made at the surgical table and there are no standardized criteria, thus it has been advocated as a surgeon-dependent risk factor for post-operative incontinence and complications. We feel to underline that the surgical technique of AUS implant is amenable of different procedural variations that influence the standardization of the technique. We partially reduced this heterogeneity with the inclusion of perineal surgical access only, but there still remains variability in terms of site of cuff implant (bladder neck or bulbar urethra), number of cuffs implanted (single or double) and cuff size.

In a prospective multicentre cohort including 386 patients, the positioning of a 3.5 cm cuff was related to a higher risk of device explantation. [36]. However, in a retrospective cohort of 1082 patients, a cuff

greater than 5.0 cm was also associated with a higher revision rate compared to smaller sizes (HR 2.91, 95%CI 1.92-4.25, $p < 0.001$) due to an increased number of complications [37].

In partial agreement with our results, in a study of 56 patients the use of a double cuff implant did not result in improved long term continence nor in quality of life. Furthermore, the rate of complications was doubled in the population implanted with double cuff (7 vs. 12 events). In another group of 180 patients it was demonstrated that no significant objective improvement on postoperative daily pad use (continence 71% single cuff, 83% double cuff, p.0.05), however patients seemed to be better satisfied with a double cuff implant (superior subjective cure rate: 78% single cuff vs. 91% double cuff, p 0.02; superior social continence: 84% single cuff vs. 98% double cuff, p 0.001) even if at the expected of a higher risk of device explantation [24,38].

With our findings, we demonstrated that a higher institutional caseload reduces the impact of operator-dependent factors on outcome.

Data on antibiotic therapy were available only for 621 patients. Antibiotic use lacks of a standard procedure for all centers, as its choice is influenced by local resistance trends and local protocols. Perioperative antibiotic prophylaxis has been demonstrated to be effective in reducing infections rates, based on studies on orthopedic prosthetic surgery [39]. However, recently, Adamsky et al. evidenced in a large cohort of 3594 AUS implants that nearly one third of patients (61.1%) are prescribed postoperative antibiotic therapy and that it does not reduce the odds of AUS explant [40].

Diabetes mellitus is a reported risk factor for prosthesis infection [41]. Anticoagulant therapy is a known risk factor for bleeding complications, which in turn, can lead to infection and erosion. Very few data are available on the correlation of anticoagulation therapy and AUS outcomes. A recent study conducted on 506 patients demonstrated that DM was associated with a higher incidence of impaired wound healing after AUS implant (7.3 vs. 1.7%, p=0.003), but no correlation to dry rate and revision

rate was reported [42]. Another cohort of AUS patients (n=954) showed that among diabetic patients, the incidence of infection and erosions at 5 years was higher compared to those without diabetes (13% vs. 8%; p=0.025); however, there was no difference between diabetic patients and controls in terms of social continence (45% vs. 57%; P=0.29) and subjective satisfaction (95% vs. 90%; p=0.43) [41].

Our overall and specific complication rate is in line with a recently published review on AUS safety: infection rate ranged from 0.5 to 10.6%, erosion rate ranged from 2.9% to 12%, urethral atrophy rates ranged from 1.6% to 11.4%, mechanical failure rates ranged between 5% and 29% [17], [37]. Lai et al. demonstrated that infection and erosion tend to be early events with a mean time to event of 3.7 and 19.8 months respectively; atrophy and mechanical failure tend to be late events with a mean time to event of 29.6 and 68.1 months respectively. Although the risks of infection and erosion reached a plateau over time, the risks of urethral atrophy and mechanical failure increased over time, as they are related to the compressive effect of the device and deterioration of mechanical components [12,34].

Several aspects of our data are noteworthy. This is the largest retrospectively collected cohort of men undergoing primary AUS with medium-term follow-up reported in the literature. By including only "virgin" AUS implants, our study eliminates possible confounding factors from re-interventions. All patients were counseled in a tertiary referral center for the surgical treatment of incontinence, and we were able to prove that even among tertiary referral centers there is a significant variability in terms of outcomes according to the number of implants performed per year. This underlines the need for accurate counseling of the patient.

The study also has some limitations. First, data were collected retrospectively from patients and surgeons' reports and some collection bias cannot be excluded. We included in the database only patients with complete data on continence and complications at last follow-up, with a possible selection bias; the success rates only accounts for patients with the device in place at least 1 year. No

standardized method was used to assess the severity of incontinence pre-operatively or the urinary outcomes after surgery. We had no information on the follow-up regimen for each center; the analysis was made on data available at last follow up.

CONCLUSION

This multicenter study has shown continence outcomes in line with previous studies, defining AUS as an effective treatment for moderate to severe male (post-prostatectomy) SUI with complete continence in 58% of patients. We report PIS as a risk factor for decreased efficacy of surgery. Revision rate (30.7% after mid-term follow-up) was impacted by Institutional caseload but not by other patient characteristics. These results should be confirmed by an international prospective study. The SATURN registry [43] should hopefully rectify this.

REFERENCES

[1] Ficarra V, Novara G, Artibani W, Cestari A, Galfano A, Graefen M, et al. Retropubic, laparoscopic, and robot-assisted radical prostatectomy: a systematic review and cumulative analysis of comparative studies. European Urology 2009;55:1037–63. doi:10.1016/j.eururo.2009.01.036.

[2] Abrams P, Cardozo L, Wagg A WA. 6th International Consultation on Incontinence / International Consultation on Urological Diseases. Paris. Health Publication Ltd 2017.

[3] Burkhard F, Bosch J, Cruz F, Lemack G, Nambiar A, Thiruchelvam N, et al. Urinary Incontinence in Adults EAU Guidelines on n.d.

[4] Silva LA, Andriolo RB, Atallah ÁN, da Silva EMK. Surgery for stress urinary incontinence due to presumed sphincter deficiency after prostate surgery. The Cochrane Database of Systematic Reviews 2014;9:CD008306. doi:10.1002/14651858.CD008306.pub3.

[5] Lucas MG, Bosch RJL, Burkhard FC, Cruz F, Madden TB, Nambiar AK, et al. EAU guidelines on surgical treatment of urinary incontinence. European Urology 2012;62:1118–29. doi:10.1016/j.eururo.2012.09.023.

[6] Herschorn S, Bruschini H, Comiter C, Grise P, Hanus T, Kirschner-Hermanns R, et al. Surgical treatment of stress incontinence in men. Neurourol Urodyn 2010;29:179–90. doi:10.1002/nau.

[7] Rothschild J, Chang Kit L, Seltz L, Wang L, Kaufman M, Dmochowski R, et al. Difference between urethral circumference and artificial urinary sphincter cuff size, and its effect on postoperative incontinence. The Journal of Urology 2014;191:138–42. doi:10.1016/j.juro.2013.06.052.

[8] Holm HV, Fosså SD, Hedlund H, Dahl AA. Study of generic quality of life in patients operated on for post-prostatectomy incontinence. International Journal of Urology : Official Journal of the Japanese Urological Association 2013;20:889–95. doi:10.1111/iju.12077.

[9] Trigo Rocha F, Gomes CM, Mitre AI, Arap S, Srougi M. A prospective study evaluating the efficacy of the artificial sphincter AMS 800 for the treatment of postradical prostatectomy urinary incontinence and the correlation between preoperative urodynamic and surgical outcomes. Urology 2008;71:85–9. doi:10.1016/j.urology.2007.09.009.

[10] O'Connor RC, Nanigian DK, Patel BN, Guralnick ML, Ellision LM, Stone AR. Artificial urinary sphincter placement in elderly men. Urology 2007;69:126–8. doi:10.1016/j.urology.2006.09.021.

[11] Ramsay AK, Granitsiotis P, Conn IG. The use of the artificial urinary sphincter in the West of Scotland: a single centre 10-year experience. Scottish Medical Journal 2007;52:14–7.

[12] Lai HH, Hsu EI, Teh BS, Butler EB, Boone TB. 13 years of experience with artificial urinary sphincter implantation at Baylor College of Medicine. The Journal of Urology 2007;177:1021–5. doi:10.1016/j.juro.2006.10.062.

[13] Walsh IK, Williams SG, Mahendra V, Nambirajan T, Stone AR. Artificial urinary sphincter implantation in the irradiated patient: safety, efficacy and satisfaction. BJU International 2002;89:364–8.

[14] Gousse AE, Madjar S, Lambert MM, Fishman IJ. Artificial urinary sphincter for post-radical prostatectomy urinary incontinence: long-term subjective results. The Journal of Urology 2001;166:1755–8.

[15] Gomes CM, Broderick GA, Sánchez-Ortiz RF, Preate D, Rovner ES, Wein AJ. Artificial urinary sphincter for post-prostatectomy incontinence: impact of prior collagen injection on cost and clinical outcome. The Journal of Urology 2000;163:87–90.

[16] Singh G, Thomas DG. Artificial urinary sphincter for post-prostatectomy incontinence. British Journal of Urology 1996;77:248–51.

[17] James MH, McCammon KA. Artificial urinary sphincter for post-prostatectomy incontinence: a

review. International Journal of Urology : Official Journal of the Japanese Urological Association 2014;21:536–43. doi:10.1111/iju.12392.

[18] Rehder P, Haab F, Cornu J-N, Gozzi C, Bauer RM. Treatment of postprostatectomy male urinary incontinence with the transobturator retroluminal repositioning sling suspension: 3-year follow-up. European Urology 2012;62:140–5. doi:10.1016/j.eururo.2012.02.038.

[19] Van Der Aa F, Drake MJ, Kasyan GR, Petrolekas A, Cornu JN. The artificial urinary sphincter after a quarter of a century: A critical systematic review of its use in male non-neurogenic incontinence. European Urology 2013;63:681–9. doi:10.1016/j.eururo.2012.11.034.

[20] Van Bruwaene S, De Ridder D, Van Der Aa F. The use of sling vs sphincter in post-prostatectomy urinary incontinence. BJU International 2015;116:330–42. doi:10.1111/bju.12976.

[21] Imamoglu MA, Tuygun C, Bakirtas H, Yiğitbasi O, Kiper A. The comparison of artificial urinary sphincter implantation and endourethral macroplastique injection for the treatment of postprostatectomy incontinence. European Urology 2005;47:209–13. doi:10.1016/j.eururo.2004.08.019.

[22] Mottet N, Boyer C, Chartier-Kastler E, Ben Naoum K, Richard F, Costa P. Artificial urinary sphincter AMS 800 for urinary incontinence after radical prostatectomy: the French experience. Urologia Internationalis 1998;60 Suppl 2:25–9; discussion 35.

[23] Van Bruwaene S, De Ridder D, Van der Aa F. The use of sling vs sphincter in post-prostatectomy urinary incontinence. BJU International 2015;116:330–42. doi:10.1111/bju.12976.

[24] Ahyai SA, Ludwig TA, Dahlem R, Soave A, Rosenbaum C, Chun FK-H, et al. Outcomes of single- vs double-cuff artificial urinary sphincter insertion in low- and high-risk profile male patients with severe stress urinary incontinence. BJU International 2016;118:625–32.

doi:10.1111/bju.13449.

[25] Farag F, van der Doelen M, van Breda J, D'Hauwers K, Heesakkers J. Decline in artificial urinary sphincter survival in modern practice-Do we treat a different patient? Neurourology and Urodynamics 2016. doi:10.1002/nau.23110.

[26] Yafi FA, DeLay KJ, Stewart C, Chiang J, Sangkum P, Hellstrom WJG. Device survival following primary implantation of the AMS 800 artificial urinary sphincter for male stress urinary incontinence. The Journal of Urology 2016. doi:10.1016/j.juro.2016.08.107.

[27] Imamoglu MA, Tuygun C, Bakirtas H, Yiğitbasi O, Kiper A. The comparison of artificial urinary sphincter implantation and endourethral macroplastique injection for the treatment of postprostatectomy incontinence. European Urology 2005;47:209–13. doi:10.1016/j.eururo.2004.08.019.

[28] Liss MA, Osann K, Canvasser N, Chu W, Chang A, Gan J, et al. Continence definition after radical prostatectomy using urinary quality of life: evaluation of patient reported validated questionnaires. The Journal of Urology 2010;183:1464–8. doi:10.1016/j.juro.2009.12.009.

[29] Bates AS, Martin RM, Terry TR. Complications following artificial urinary sphincter placement after radical prostatectomy and radiotherapy: a meta-analysis. BJU International 2015;116:623–33. doi:10.1111/bju.13048.

[30] Kaufman MR, Milam DF, Johnsen N V, Cleves MA, Broghammer JA, Brant WO, et al. Prior Radiation Therapy Decreases Time to Idiopathic Erosion of Artificial Urinary Sphincter: A Multi-Institutional Analysis. The Journal of Urology 2018;199:1037–41. doi:10.1016/j.juro.2017.11.046.

[31] Radomski SB, Ruzhynsky V, Wallis CJD, Herschorn S. Complications and Interventions in Patients with an Artificial Urinary Sphincter: Long-Term Results. The Journal of Urology 2018. doi:10.1016/j.juro.2018.05.143.

[32] Abdou A, Cornu J-N, Sèbe P, Ciofu C, Peyrat L, Cussenot O, et al. [Salvage therapy with artificial urinary sphincter after Advance™ male sling failure for post-prostatectomy incontinence: a first clinical experience]. Progres En Urologie : Journal de l'Association Francaise D'urologie et de La Societe Francaise D'urologie 2012;22:650–6. doi:10.1016/j.purol.2012.06.011.

[33] Ajay D, Zhang H, Gupta S, Selph JP, Belsante MJ, Lentz AC, et al. The Artificial Urinary Sphincter is Superior to a Secondary Transobturator Male Sling in Cases of a Primary Sling Failure. The Journal of Urology 2015;194:1038–42. doi:10.1016/j.juro.2015.04.106.

[34] Lai HH, Boone TB. The surgical learning curve of artificial urinary sphincter implantation: implications for prosthetic training and referral. The Journal of Urology 2013;189:1437–43. doi:10.1016/j.juro.2012.10.116.

[35] Sandhu JS, Maschino AC, Vickers AJ. The surgical learning curve for artificial urinary sphincter procedures compared to typical surgeon experience. European Urology 2011;60:1285–90. doi:10.1016/j.eururo.2011.05.048.

[36] Brant WO, Erickson BA, Elliott SP, Powell C, Alsikafi N, McClung C, et al. Risk factors for erosion of artificial urinary sphincters: a multicenter prospective study. Urology 2014;84:934–8. doi:10.1016/j.urology.2014.05.043.

[37] Linder BJ, Rivera ME, Ziegelmann MJ, Elliott DS. Long-term Outcomes Following Artificial Urinary Sphincter Placement: An Analysis of 1082 Cases at Mayo Clinic. Urology 2015;86:602–7. doi:10.1016/j.urology.2015.05.029.

[38] O'Connor RC, Lyon MB, Guralnick ML, Bales GT. Long-term Follow-up of Single Versus Double Cuff Artificial Urinary Sphincter Insertion for the Treatment of Severe Postprostatectomy Stress Urinary Incontinence. Urology 2008;71:90–3. doi:10.1016/j.urology.2007.08.017.

[39] Van der Aa F, Drake MJ, Kasyan GR, Petrolekas A, Cornu J-N. The Artificial Urinary Sphincter After a Quarter of a Century: A Critical Systematic Review of Its Use in Male Non-neurogenic Incontinence. European Urology 2013;63:681–9. doi:10.1016/j.eururo.2012.11.034.

[40] Adamsky MA, Boysen WR, Cohen AJ, Ham S, Dmochowski RR, Faris SF, et al. Evaluating the Role of Postoperative Oral Antibiotic Administration in Artificial Urinary Sphincter and Inflatable Penile Prosthesis Explantation: A Nationwide Analysis. Urology 2018;111:92–8. doi:10.1016/j.urology.2017.07.064.

[41] Viers BR, Linder BJ, Rivera ME, Andrews JR, Rangel LJ, Ziegelmann MJ, et al. The Impact of Diabetes Mellitus and Obesity on Artificial Urinary Sphincter Outcomes in Men. Urology 2016. doi:10.1016/j.urology.2016.06.038.

[42] Hüsch T, Kretschmer A, Thomsen F, Kronlachner D, Kurosch M, Obaje A, et al. Risk Factors for Failure of Male Slings and Artificial Urinary Sphincters: Results from a Large Middle European Cohort Study. Urologia Internationalis 2016. doi:10.1159/000449232.

[43] Hamid Rizwan. Prospective Registry for Patients Undergoing Surgery for Male Stress Urinary Incontinence in Multiple European Centres EAU-RF 2016-01 n.d.

Reviewer: 1

1. The only information needed for a time-event model, such as a Kaplan Meier analysis, is the time to last follow-up and whether the patient is censored or was a failure at that time point. Thus, performing the analysis should be feasible, even in the current dataset. This would be a useful addition to the paper.

Thank you for your comment. Since we have data on time to last follow-up we could perform the analysis on the dry rate over time as you suggested. This was not possible for revision rate since we don't have data on time to revision. We included figure number 2 with the Kaplan Meier analysis.

2. Excluding patients that failed before 12 months, for instance those that had an infection in the first few months, will artificially inflate the success rates. Would add this as a limitation, that the success rates only account for patients with the device in place at least 1 year.

Thank you for your comment. We included this limitation in line 254.

3. Would remove the comment that the study included "single surgical teams" for each institution, since it is overly vague. The authors report that they can't specify the number of surgeons that performed the cases at each institution. It is likely there were multiple surgeons and thus, multiple surgical teams.

Thank you for your comment. We removed the comment from line 51.

TABLE 1

Comparison between groups according to pre-operative and intra-operative variables

Variable	Overall (n=892)	Radical Prostatectomy (n=766)	TURP (n=126)	p
Age Mean-median (Range)	68 – 68 (39-87)	68-69 (41-87)	67-67 (39-82)	0.76
RT N (%)	257 (28.9%)	219 (28.6%)	38 (30.1%)	0.40
PIS N (%)	218 (24.4%)	187 (24.4%)	31 (24.6%)	0.52
DM N (%)	111 (12.4%)	88 (11.5%)	23 (18.2%)	0.02
AC N (%)	217 (27.4%)	178 (23.2)	39 (30.9%)	0.03
DOUBLE CUFF N (%)	83 (9.3%)	74 (9.6%)	9 (7.1%)	0.23
CUFF size 3.5 4.0 4.5 5.0 5.5 6.0 6.5	 30 (3.4%) 271 (30.4) 415 (46.5%) 99 (11.1%) 35 (4.0%) 10 (1.1%) 4 (0.4%)	 26 (3.4%) 239 (31.2%) 352 (46.0%) 89 (11.6%) 28 (3.7%) 6 (0.8%) 4 (0.5%)	 4 (3.2%) 32 (25.3%) 63 (50.0%) 10 (7.9%) 8 (6.3%) 4 (3.2%) -	0.71

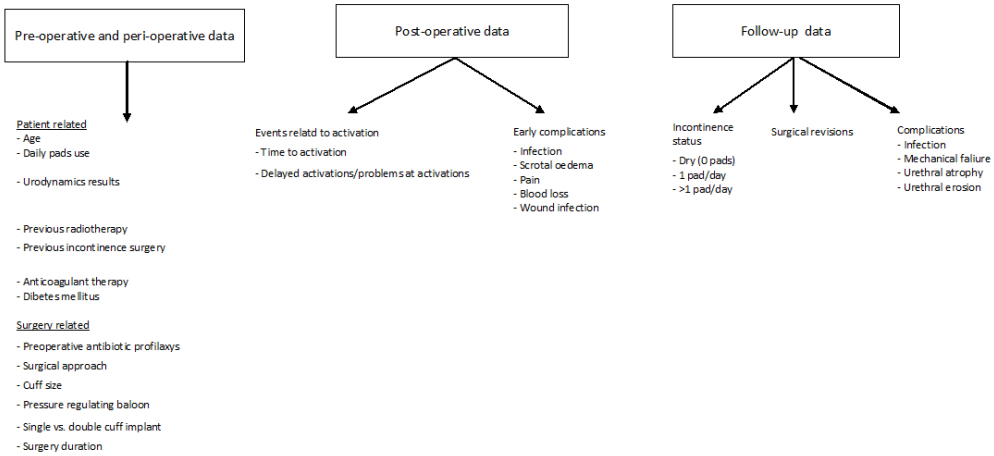
RT: radiotherapy; PIS: previous incontinence surgery, DM: diabetes mellitus, AC: anticoagulation therapy.

TABLE 2
Multivariable logistic regression analysis predicting dry rate and freedom from surgical revision (CI: 95%)

	DRY RATE		FREEDOM FROM REVISION	
Variable	**OR**	**p**	**OR**	**p**
Age	0.99	0.38	1.02	0.29
RT	1.24	0.21	1.32	0.13
DM	1.22	0.37	1.23	0.38
AC	1.18	0.34	1.39	0.09
PIS	0.51	0.03	0.79	0.30
DOUBLE CUFF	0.61	0.07	0.79	0.68
CUFF size	0.90	0.54	0.87	0.39
ICL	1.18	0.005	1.51	0.00

RT: radiotherapy; PIS: previous incontinence surgery, DM: diabetes mellitus, AC: anticoagulation therapy, ICL: institutional case load.

FIG.1 Common template of collected data

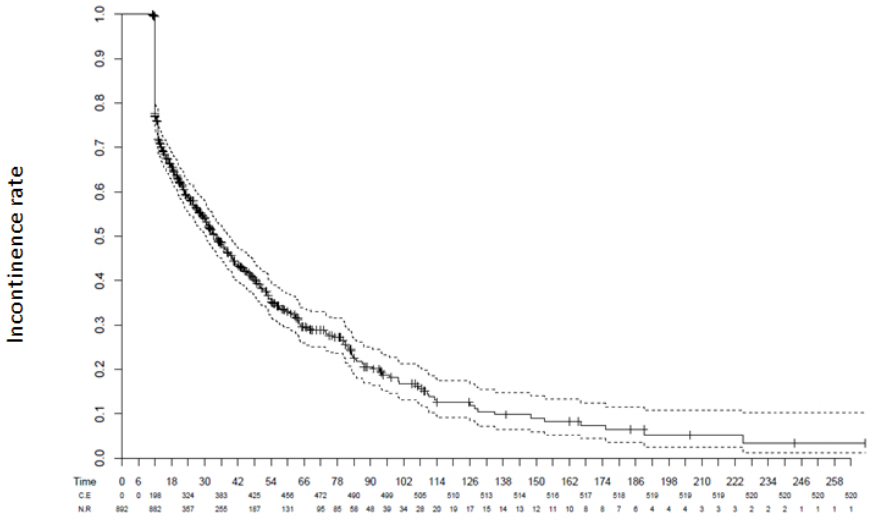


Common template of collected data

286x186mm (96 x 96 DPI)

Figure 2

Kaplan-Meier estimate of incontinence rate after surgery over time



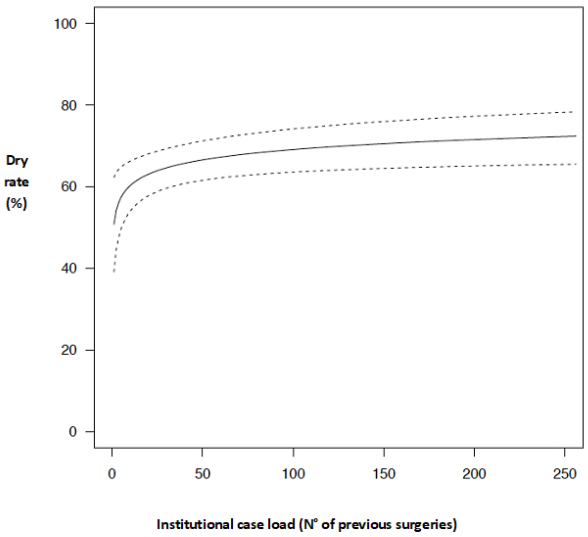
N.R. Number at risk; C.E. Cumulative events

Kaplan-Meier estimate of incontinence rate after surgery over time

216x166mm (96 x 96 DPI)

FIG.3

Adjusted differences in dry rate according to institutional case load

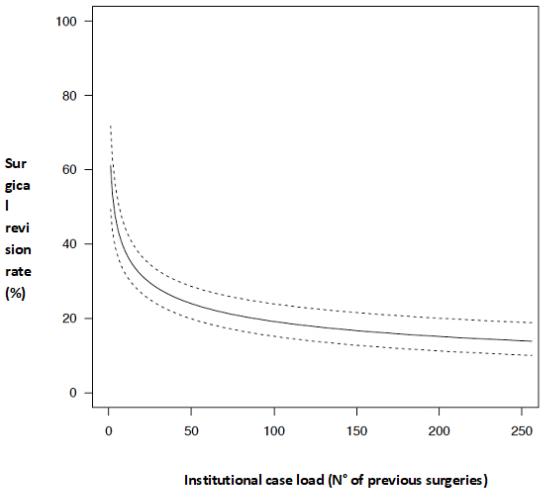


Adjusted differences in dry rate according to institutional case load

270x176mm (96 x 96 DPI)

FIG.4

Adjusted differences in surgical revision according to institutional case load



Adjusted differences in surgical revision according to institutional case load

267x178mm (96 x 96 DPI)