UNIVERSITÉ DE LILLE

FACULTE DE MÉDECINE HENRI WAREMBOURG

Année : 2020

THÈSE POUR LE DIPLOME D'ÉTAT
DE DOCTEUR EN MÉDECINE

BALLONS ACT® (ADJUSTABLE CONTINENCE THERAPY) ET INCONTINENCE URINAIRE DE LA FEMME : EFFICACITE, COMPLICATIONS, FACTEURS DE RISQUE D'ECHEC ET DE COMPLICATIONS.

Présentée et soutenue publiquement le 10 Juin 2020 à 18h
au Pôle Recherche

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INTRODUCTION

L'incontinence urinaire (IU) est un problème de santé publique majeur puisqu'il concerne 25% à 45% des femmes [1]. Cette pathologie impacte de manière significative la qualité de vie des patientes [2] et représente un réel fardeau économique pour elles et la société [3] . Selon la Société Internationnale de l'Incontinence (ICS), l'incontinence urinaire d'effort (IUE) est définie comme étant « une perte involontaire d'urine à l'effort, lors d'une activité physique, d'un éternuement ou d'une toux » [4]. Pour 50% des femmes ayant une incontinence urinaire, l'incontinence urinaire d'effort (IUE) est un symptôme isolé ou initial de leur incontinence [5]. L'IUE est due anatomiquement à une hypermobilité uréthrale et/ou du col vésical ou à une insuffisance sphinctérienne (IS). En réalité, les deux mécanismes sont sans doute combinés et associés à d'autres symptômes du bas appareil urinaire.

Pour corriger l'IUE, une prise en charge chirurgicale est habituellement proposée après échec des traitements conservateurs, comme la rééducation périnéale. Les options chirurgicales possibles et leur place dans l'algorithme du traitement de l'IUE varient significativement selon les recommandations auxquelles on se réfère [6]. Selon les recommandations internationnales sur l'incontinence urinaire chez la femme, la colposuspension, les bandelettes sous-uréthrales, les agents de comblement périuréthraux sont proposés de façon systématique et discutés, alors que d'autres techniques chirurgicales, comme le sphincter urianire artificiel (SUA) ou les ballons ACT®, sont rarement mentionnées.

Les bandelettes sous-uréthrales ont d'excellents résultats avec un succès à long terme allant jusqu'à 90% [7]. Cette technique chirurgicale est la plus utilisée pour traiter l'IUE chez la femme mais uniquement s'il s'agit d'une IUE avec hypermobilité uréthrale. Elle est donc proposée en chirurgie de première ligne mais rarement pour une IU récurrente en particulier si l'urèthre est fixe. Les agents de comblement, avec un taux de succès à 26%, ont une efficacité limitée mais offre une solution aux patientes âgées, ayant un risque anesthésique élevé ou réticentes pour une option chirurgicale [8].

Le SUA est utilisé depuis plusieurs années pour traiter l'IUE féminine avec IS, donnant de bons résultats avec un taux de continence parfaite allant de 42% à 86% après un suivi moyen de 69 mois [9]. Cette chirurgie est de plus en plus proposée depuis les dix dernières années [10], notamment en raison de l'émergence de la laparoscopie robot-assistée. Cependant elle est toujours considérée comme une chirurgie invasive puisqu'elle est pourvoyeuse de complications graves concernant la procédure (2% à 54%). Il existe également des complications graves dues au matériel, comme l'explantation (2% à 27%), ainsi que des dysfonctionnement mécaniques (2% à 41%) nécessitant des révisions chirurgicales fréquents (6% à 44%) [9].

Dans une moindre mesure, les ballons ACT® sont proposés dans plusieurs pays pour traiter l'IUE avec IS prédominante ou isolée. Les recommandations de l'EAU concernant l'incontinence urinaire chez la femme positionnent les ballons ACT® et le SUA au même niveau pour traiter l'IUE compliquée [11]. Bien qu'il n'y ait pas eu d'étude comparative prospective, les ballons ACT® semblent être moins efficaces que le SUA. Dans une revue systématique incluant 8 études - 610 patientes , après un suivi moyen de 12 à 72 mois, seulement 15% à 44 % des patientes implantées par ballons ACT® se considéraient guéris, et 66% à 78.4 % étaient satisfaits et améliorés [12]. Dans une étude comparative rétrospective récente, Freton et al. montraient une différence statistiquement significative concernant la continence totale à 6 mois en faveur du SUA versus ballons ACT® (71.4% vs 21.7%, $p<0.001$). A 6 mois de l'implantation, les patientes se disaient améliorées ou très améliorées pour 40% des ballons ACT® et 83.3% des SUA [13].
Cependant, les ballons ACT® peuvent être considérés comme moins invasifs que le SUA. En effet, implantés par une voie d'abord périnéale minime, ils ont un plus faible taux d'effets indésirables graves et aucune complication majeure n'a été rapportée [12]. Ceci est confirmé par Freton et al. qui rapportent une dimininution significative des complications per-opératoires des ballons ATC® par rapport au SUA (8% vs 47%, $p < 0.001$) [13].

L’évaluation de l’efficacité et des complications des ballons ACT® est restreinte chez la femme avec seulement 10 études publiées. Leur interprétation est principalement limitée par un faible nombre de patientes et une durée de suivi variable. Bien que les facteurs de rique d’échec et de complications soient bien identifiés pour le SUA , avec l’âge>70ans, une précédente chirurgie de l’incontinence urinaire, un antécédent de colposuspension, la radiothérapie pelvienne ou une vessie neurologique [14,15], aucun n’a été reconnu ni recherché pour les ballons ACT®.

La place des ballons ACT® dans l’algorithme du traitement de l’IUE de la femme, principalement si l’IS est majeure, est encore ambigüe. Sa position par rapport aux autres traitements de l’IS de la femme, comme le SUA, peut être mieux définie si l’efficacité, les complications et les facteurs de risque d’échec et de complications sont étudiés et clairement identifiés.

Les objectifs de cette étude sont d’évaluer l'efficacité et les complications chirurgicales des ballons ACT® dans la prise en charge de l’IU d’effort ou mixte chez la femme, et de rechercher leurs facteurs de risque d’échec et de complications chirurgicales à court terme.

DISCUSSION

Dans notre étude, 37% et 33.5% des patientes se condidéraient guéris ou améliorés un an après l'implantation des ballons ACT®. Des complications chirurgicales ont été rapportées chez 36.1% des patientes, avec 4.8% de complications per-opératoires et 32.5% de complications post-opératoires. Vingt-six pourcents des patientes ont du être explantés, et 50.6% d'entre-elles ont pu être ré-implantés. Après un suivi uniforme de 1 an, nous n'avons pas retrouvé de facteur de risque associé à un échec à court terme ou à une complication chirurgicale.

Concernant l'efficacité, nos résultats concordent avec ceux rapportés dans la littérature avec un taux de succès allant de 15% à 44%, et d'amélioration globale de 66% à 78.4% [12].
L'absence de facteur de risque d'échec retrouvée dans de notre importante cohorte féminine remet en question ceux évoqués dans d'autres séries. La sévérité de l'incontinence [16] ou la radiothérapie externe [17] ont été rapportés dans une population masculine ou mixte. Chez les femmes, seule l'obésité a été évoquée comme facteur de rique d'échec [18]. Cette hypothèse a été réfutée par Vayleux et al. [14] qui rapportaient un taux de succès après implantation de ballons ACT équivalent entre les femmes obèses et non-obèses. Dans une revue systématique sur l'obésité et l'IUE de la femme, Osbourn et al.[19] retrouvaient également un taux de succès identique chez les femmes obèses ou non-obèses ayant eu une chirurgie d'incontinence urinaire.

Concernant la survenue de complications, nos résultats concordent avec ceux déjà publiés. Dans la littérature récente, les complications per-opératoire survenaient dans 3.7% à 4.5% des cas, et les complications post-opératoire à un an étaient plus fréquentes, comptant l'érosion uréthrale (2-15%), l'érosion cutanée du port (3–7.5 %),

la migration de ballon (6.5–17.5 %), l'infection du matériel (0.6–8.9 %) et la dysfonction du ballon (0.6–6 %) [12].Abosseif et al. retrouvent un taux de réimplantation de 50% identique à celui de notre série [20,21]. La réimplantation n'entrave pas les résultats fonctionnels et 2/3 des patientes retrouvent une continence totale ou améliorée.
Aucun facteur de risque de complications n'a émergé de notre série. Les facteurs de risque retrouvés dans la littérature, comme la radiothérapie pelvienne, concernent des populations masculines ou mixtes et n'ont jamais été isolés dans une populations strictement féminine. Chez l'homme, la radiothérapie pelvienne permet de traiter le plus fréquement un cancer de prostate, alors qu'elle est utilisée chez la femme pour les cancers du col de l'utérus, de l'endomètre ou colo-rectal. L'irradiation diffère en terme de champ et de dose, et entraîne donc des conséquences différentes sur l'environnement péri-urétral. Cela expliquerait que l'antécédent de radiothépie pelvienne soit un facteur de risque démontré chez l'homme et non chez la femme.

Les recommandations de l'EAU sur le traitement chirurgicale de l'incontience urinaire de la femme réservent les ballons ACT® pour le traitement de l'IU compliquée, au même niveau que le SUA. Les ballons ACT® et le SUA présentent clairement des profils d'efficacité et de complications distincts. Certes les ballons ACT® ont une efficacité limitée comparés au SUA, mais ils présentent un taux bien plus faible de complications, le plus souvent mineures facilement prises en charge avec une explantation possibleen ambulatoire voire sous simple anesthésie locale.

Bien que plusieurs facteurs de risque d'échec et de complications soient connus pour le SUA, aucun n'a été jusqu'alors identifié pour les ballons ACT® chez la femme et nos résultats convergent dans ce sens. Ainsi notre étude aide à clarifier la place des ballons ACT® dans l'arsenal thérapeutique de l'IUE de la femme. Il peut donc être recommandé de ne pas restreindre leur indication chez la femme, et même de promouvoir leur utilisation pour des patientes présentant des facteurs de risque d'implantation de SUA.

Notre étude est statistiquement puissante et optimisée par un design multicentrique. Cependant certaines plusieurs limites et faiblesses doivent être soulignées, comme son recueil rétrospectif- entrainant un manque de données récurrant- ou sa courte durée de suivi. De plus, le critère de jugement composite, combinant une évaluation objective et subjective pourtant appropriée pour une chirurgie fonctionnelle, n'est pas encore validé.

Nos résultats doivent être confirmés par une étude prospectif évaluant les résultats à plus long terme. Un essai randomisé prospectif comparatif avec le SUA est en cours et aidera sans aucun doute la communauté urologique à mieux placer les ballons ACT® dans l'algorithme futur du traitement de l'IUE de la femme[22].

CONCLUSION

Aucun facteur de risque d'échec ou de complication post-opératoire des ballons ACT® chez la femme n'a pu être identifié. Malgré son efficacité limitée, cette technique mini-invasive a une bonne balance bénéfice/risque avec des complications locales facilement prises en charge. Les ballons ACT® ne devraient pas être réservés à une population restreinte, mais pourraient être proposés à toutes les patientes présentant une IU d'effort ou mixte avec insuffisance sphinctérienne, quelques soient leurs comorbidités ou antécédent médical et chirurgical.

MANUSCRIT ANGLAIS

ADJUSTABLE CONTINENCE THERAPY (ACT®) BALLOONS AND FEMALE URINARY INCONTINENCE: EFFICACY, SAFETY AND RISK FACTORS FOR FAILURE AND COMPLICATIONS

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Key words:
Female urinary incontinence, Sphincter deficiency, Periurethral balloons, ACT® balloons, Urinary prosthesis, Safety, Postoperative complications

Abbreviations and Acronyms:
ACT® Adjustable Continence Therapy
SUI stress urinary incontinence
ISD intrinsic sphincter deficiency
NRS numeral rating scale NRS
PPD pad(s) per day
AUS artificial urinary sphincter
ICS International Continence Society
OAB OverActivite Bladder

ABSTRACT

Purpose

To assess efficacy and safety as well as risk factors for failure and complications associated with Adjustable Continence Therapy (ACT®) balloons in women.

Materials and Methods

In the present retrospective multicentric cohort study, all women implanted with ACT® balloons to treat mixed or stress urinary incontinence between 2000 and 2018 were considered for inclusion. Efficacy was assessed one year after implantation, and women were allocated in three different groups as follows: Success - maximum 1 pad per day and patient's impression of improvement assessed using a numeral rating scale (NRS) ≥ 8/10. Improvement - decrease of daily pad use and/or NRS ≥ 5/10. Failure - increase or stability of daily pad use day or NRS < 5/10. Complications were assessed one year after implantation, and classified as per-operative and early or late post- operative complications. In parallel, we assessed risk factors for failure and post-operative surgical complications, collecting epidemiological data, medical, surgical and obstetrical history as well as clinical and urodynamic data.

Results

Among the 281 included women, with a median age of 71.0 years (61.0 ; 77.0) , 104 (37.0%) and 94 (33.5%) reported success and improvement, respectively, while 83 (29.5%) reported failure. Per-operative as well as early and/or a late post-operative complications occurred in 99 women (36.1%), and 75 women (26,7%) finally underwent a uni or a bilateral explantation. No major complication was reported. None of the studied risk factors were statistically associated with failure or complication.

Conclusion

No risk factor was identified to predict short-term failure or complications associated with ACT® balloons in women. This mini-invasive device, even if limited in efficacy, may therefore not be restrained to a selected population, and could be safely proposed in all patients presenting with mixed or stress urinary incontinence, especially when intrinsic sphincter deficiency is the predominant mechanism.

INTRODUCTION

Urinary incontinence (UI), considered as a significant health problem concerning 25% to 45% of women woldwide[23], is associated with a significant impact on female quality of life[2] as well as a substantial economic burden for patients and society[3]. According to the International Continence Society (ICS), stress urinary incontinence (SUI) is defined as ‘‘the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing’’[4]. About 50% of women with UI report SUI as the primary or sole symptom of incontinence[5]. SUI is due to excessive mobility of the urethra (or bladder neck) or intrinsic sphincter deficiency (ISD). In reality the both are é and combined with other lower urinary tract symptoms[4].

To correct SUI, surgical management is usually proposed after conservative strategies, such as pelvi floor muscle training, have failed. Available surgical options and their respective place in SUI treatment algorithm can vary significantly according to the “guidelines” considered[6]. Among international guidelines focusing on female urinary incontinence, colposusension, mid-uretral tape and periurethral bulking agents are systematically proposed and discussed, while other surgical procedures, such as artificial urinary sphincter (AUS) or adjustable continence therapy (ACT®) balloons are rarely mentioned.

Mid-urethral tape presents excellent results, with a long-term success rate reported to be as hight as 90%[7]. This procedure is the most used to treat SUI in women but only responds to the mechanism of excessive mobility of the urethra. It is therefore considered as a first surgical line and may be rarely proposed for recurrent SUI, especially if a fixed, immobile urethra is observed. Bulking agents, with a cure rate of 26%, are associated with limited efficacy and may only be offered to women high anesthesia risk, elderly patients, or patients reluctant to undergo surgery[8].

Meanwhile, AUS has been used for many years to treat female SUI with ISD, yielding good results with a “no pad” continence rate of 42% to 86% after a mean 69-month follow-up[9]. This procedure, even if more and more proposed in the last decade[10], notably due to the increasing use of robot-assisted laparoscopy. However it may be considered as an invasive surgery since it is responsible of significant serious procedure adverse events (2% to 54%). About the device, serious adverse effects, such as explantation (2% to 27%), were reported, as well as a high mechanical dysfunction rate (2% to 41%) needing frequent surgical revisions (6% to 44%)[9].

To a lesser extent, ACT® balloons, as an external compression device, are now proposed in several countries to treat SUI with predominant or isolated ISD. EAU guidelines, focusing on surgical treatment of female urinary incontinence, even position them at the same level than AUS for women with complicated SUI[11]. Although no prospective comparison have been reported yet, ACT® balloons seem to be associated with less efficacy than AUS in this indication. Indeed, in a systematic review including 8 studies - 610 patients , after a mean-follow-up going from 12 to 72 months, only 15% to 44 % of patients implanted with ACT® balloons considered that they were cured, while 66% to 78.4 % of women were satisfied with the result and feel improved[12]. This preliminary impression is supported by a recent retrospective publication comparing ACT® balloons to AUS in the treatement of female SUI due to ISD [13]. Freton et al. reported a statistically significant three-fold decrease in complete urinary continence 6 months after ACT® balloons implantation, when compared with AUS (21.7% vs 71.4%, $p < 0.001$). Likewise, 40% and 83.3% of women feeled improved or very improved six months after ACT® balloons and AUS implantation, respectively[13].

However, ACT® balloons, implanted through a short perineal approach, have a lower serious adverse event rate - since no major complication have been reported, and may be considered, from far, as less invasive than AUS[12]. This assertion is, once more, corroborated by Freton et al., that reported a significant decrease in intra-operative complications during ACT® balloons implantation when compared with AUS implantation (8% vs 47%, $p < 0.001$)[13].

The assessment of efficacy and safety associated with ACT® balloons remains limited in the female population. Their interpretations are mainly restricted by a limited number of patients and heterogeneous length of follow-up. Furthermore, although risk factors for failure and complications have already been reported for AUS - including age >70 years, previous surgeries for urinary incontinence, history of colposuspension procedure, pelvic radiotherapy or existence of an underlying neurogenic bladder[14,15] –no one has been identified or even looked for, yet, in the case of ACT® balloons.

The place of ACT® balloons in the algorithms of female SUI treatment, especially when ISD is predominant, still remains unclear. Its position with other female ISD treatments, such as AUS, could be more precisely specified if efficacy, safety and risk factors for failure and complications were clearly assessed and identified.

The objectives of the present study were to assess short-term efficacy and safety as well as look for shotr-term risk factors for failure and surgical complications associated with ACT® balloons implantation to treat female mixed or stress UI.

MATERIALS AND METHODS

Study Design

The present work was designed as a retrospective multicentric cohort study, implicating 5 French university hospital centers and was carried out in the second half of year 2019. All women who have undergone ACT® balloons implantation to treat mixed or stress UI between January 2000 to April 2018 were considered eligible. Women presenting with a significant amount of missing data within the first post-implantation year were excluded.

Data collection

Epidemiological data, medical, surgical and obstetrical history, clinical and urodynamic data at baseline, data regarding ACT® balloons implantation procedure as well as intra- and post-operative surgical complications were retrieved from patients' paper and/or computerised medical records in accordance with the good practice guidelines of each institution.

ACT® balloons implantation procedure

A unique device known as Adjustable Continence Therapy (ACT®) balloons (Adjustable Continence Therapy, Uromedica, Inc., Plymouth, MN, USA) was used. A pre-operative negative urine culture was mandatory. The procedure consisted in placing two of these adjustable balloons on each side of the urethra, at 3 and 9 o'clock, below the bladder neck, according to the technique previously standardized by Vayleux et al. [24]. Women were installed in gynecological position under general anesthesia. The implantation was carried out through a perineal approach - a small incision was performed in the labia majora at the level of the urethra meatus - using radioscopic and endoscopic guidance. The balloons were initially filled between 0.5 to 1.5 mL with a radio-opaque isotonic solution, and injection ports were buried subcutaneously under the labia majora. Balloons adjustments began 6 weeks after implantation, and then once a fortnight until a steady-state was achieved.

Primary endpoint

The primary endpoint was the efficacy one year after implantation. Regarding efficacy, patients were allocated to three distinct groups (success, improvement and failure) according to a composite end-point elaborated using objective and subjective outcomes. The objective outcome considered the daily pad use compared to baseline, while the subjective outcome reflected the patient's impression of improvement using a 0-10 numeral rating scale (NRS). Success was defined as the presence of a maximum 1 pad per day associated with a NRS ≥ 8/10. Improvement was defined as a decrease in daily pad use and/or a NRS ≥ 5/10. Failure was defined as an increase or a stability in daily pad use or a NRS < 5/10.

Secondary endpoints

The secondary endpoints included safety as well as risk factors for failure and post-operative surgical complications associated with ACT® balloons in the year following implantation. Surgical complications were classified as intra-operative as well as early and late post-operative complications, including vaginal, urethral and bladder injuries or erosions, operative site infections, hematoma and explantation. The parameters assessed as risk factors for failure included epidemiological data (age, body mass index), medical history (diabetes, underlying neurological disease, pelvic radiotherapy, overactive bladder therapy), surgical history (anti-incontinence, prolapse surgery, other pelvic surgery), obstetrical history (parity, vaginal delivery), as well as clinical data (type of urinary incontinence, number of daily pad use) and urodynamic data (detrusor overactivity, bladder compliance disorders, maximal urethral closure pressure). The parameters assessed as risk factors for post-operative complication included epidemiological data (age, body mass index), medical history (diabetes, pelvic radiotherapy), surgical history (anti-incontinence, prolapse surgery, other pelvic surgery), obstetrical history (parity, vaginal delivery), intra-operative complication.

Statistical analysis

Continuous variables are expressed as means (standard deviation, SD) in the case of normal distribution or medians (interquartile range) otherwise. Categorical variables are expressed as numbers (percentage). Normality of distributions was assessed using histograms and the Shapiro-Wilk test.

Baseline characteristics were described between included and excluded patients and standardized differences were calculated to appreciate imbalance; standardized differences>10% were interpreted as meaningful differences.

Failure, complication and explantation rates were estimated with 95% confidence intervals (exact Clopper-Pearson method). Categorical variables were compared between patients with and without failure as well as between patients with and without complications by the Chi-square test or Fisher's exact test. Continuous variables were compared between the two groups by Mann-Whitney U-test.

Statistical testing was done at the two-tailed α-level of 0.05. Data were analyzed using SAS software (version 9.4; SAS Institute Inc., Cary, NC). Statistical analyzes were carried out by the Methodology – Biostatistics Unit of the Lille University Hospital.

RESULTS

Patients characteristics

Characteristics at baseline

A total of 358 women were implanted with ACT® balloons to treat mixed or pure stress urinary incontinence between January 2000 and April 2018 within the 5-participating university hospital centers. Among them, 77 women presented with a significant amount of missing data at the time of data collection – such as medical, surgical or obstetrical history - and were excluded. Overall, 281 patients were finally included for analysis. Included and excluded patients were comparable with a small effect size reported for all baseline data considered (Table V)

One hundred and twenty-four patients (48.8%) complained of mixed incontinence, and 48 patients (19.9%) were dispensed a concomitant overactive bladder therapy as follows: 32 (13.3%) had anticholinergic, 1 (0.4%) had β3-adrenoceptor agonist, 1 (0.4%) had intravesical botulinum toxin a, 2 (0.8%) had transcutaneous tibial nerve stimulation and 15 (6.2%) had sacral neuromodulation. Before implantation, patients had a median daily pad use of 5 pads (3.0 ; 6.0). Baseline characteristics are summarized in Table I.

Characteristics after a one-year follow-up

One year after implantation, adjustment was considered to be completed for all ACT® balloons. Mean filling volume was 3.4 ml (± 1.8) and median number of inflations was 3.0 (2.0 ; 5.0). Sixty-seven patients (31.9%) were dispensed a concomitant overactive bladder therapy as follows: 56 (26.7%) had anticholinergic, none had β3-adrenoceptor agonist, 1 (0.5%) had intravesical botulinum toxin a, 2 (1%) transcutaneous tibial nerve stimulation, 14 (6.9%) sacral neuromodulation. During this one-year follow-up, 75 patients (27%) underwent a uni- or bilateral explantation, while 38 patients (13.6%) underwent a uni- or bilateral redo procedure after explantation.

	N = 281	
Age (median, IQR)	71.0	(61.0 ; 77.0)
BMI (kg/m²) (median, IQR)	26.4	(23.0 ; 30.5)
Urinary incontinence		
Pure stress urinary incontinence (n,%)	130/254	51.2%
Mixed urinary incontinence (n,%)	124/254	48.8%
Daily pad use (median, IQR)	5.0	(3.0 ; 6.0)
History of OAB therapy		
Overall (n,%)	49/199	24.6%
Anticholinergic (n,%)	37/199	18.6%
Beta 3 agonist (n,%)	1/198	0.5%
Botulinum toxin A (n,%)	4/198	2.0%
PNTS (n,%)	2/198	2.0%
SNM (n,%)	16/198	8.1%
Vaginal prolapse		
Anterior prolapse (n,%)	12/175	6.9%
Posterior prolapse (n,%)	8/175	4.6%
Anterior et posterior prolapse (n,%)	6/175	3.4%
Medical history		
Diabetes	36/269	13.4%
Type 1	2/265	0.8%
Type 2	30/265	11.3%
Underlying neurologic disease (n,%)	51/277	18.4%
Pelvic radiation therapy (n,%)	22/275	8.0%
Pelvic cancer (n,%):		
Cervical cancer	11/274	4.0%
Endometrium cancer	4/274	1.5%
Rectum cancer	2/274	0.7%
Other cancer	5/274	1.5%
Surgical history		
Stress urinary incontinence surgery (n,%)	179/277	64.6%
Retro-pubic sub-urethral tape	97/272	35.7%
Trans-obturator sub-urethral tape	61/272	22.4%
Colposuspension	42/272	15.4%
Urethral bulking agents	7/274	2.6%
Artificial urinary sphincter	26/274	9.5%
Others	11/274	4.0%
Vaginal prolapse surgery (n,%)	86/275	31.3%
Promontofixation	56/262	21.4%
Vaginal approach	11/262	4.2%
Promontofixation+vaginal approach	6/262	2.3%
Other pelvic surgery (n,%)	128/244	52.5%
Obstetrical history		
Parity (median, IQR)	2.0	(2.0 ; 3.0)
Vaginal delivery (media, IQR)	2.0	(1.0 ; 3.0)
Urodynamic parameters		
Detrusor overactivity (n,%)	38/233	16.3%
Bladder compliance disorder (n,%)	8/189	4.2%
Qmax (mL/sec) (mean ± sd)	21.0	± 12.1
PVR (mL) (mean ± sd)	35.1	± 77.3
MUCP (cmH_2O) (mean ± sd)	25.3	± 11.9

BMI : Body mass index ; OAB: OverActive Bladder ; PTNS : Posterior tibial nerve stimulation ; SNM : Sacral nerve modulation ; Qmax : maximal uroflow; PVR : Post-void residual volume ; MUCP : Maximal urethral closure pressure ; NA : Non applicable; IQR: interquartile range.

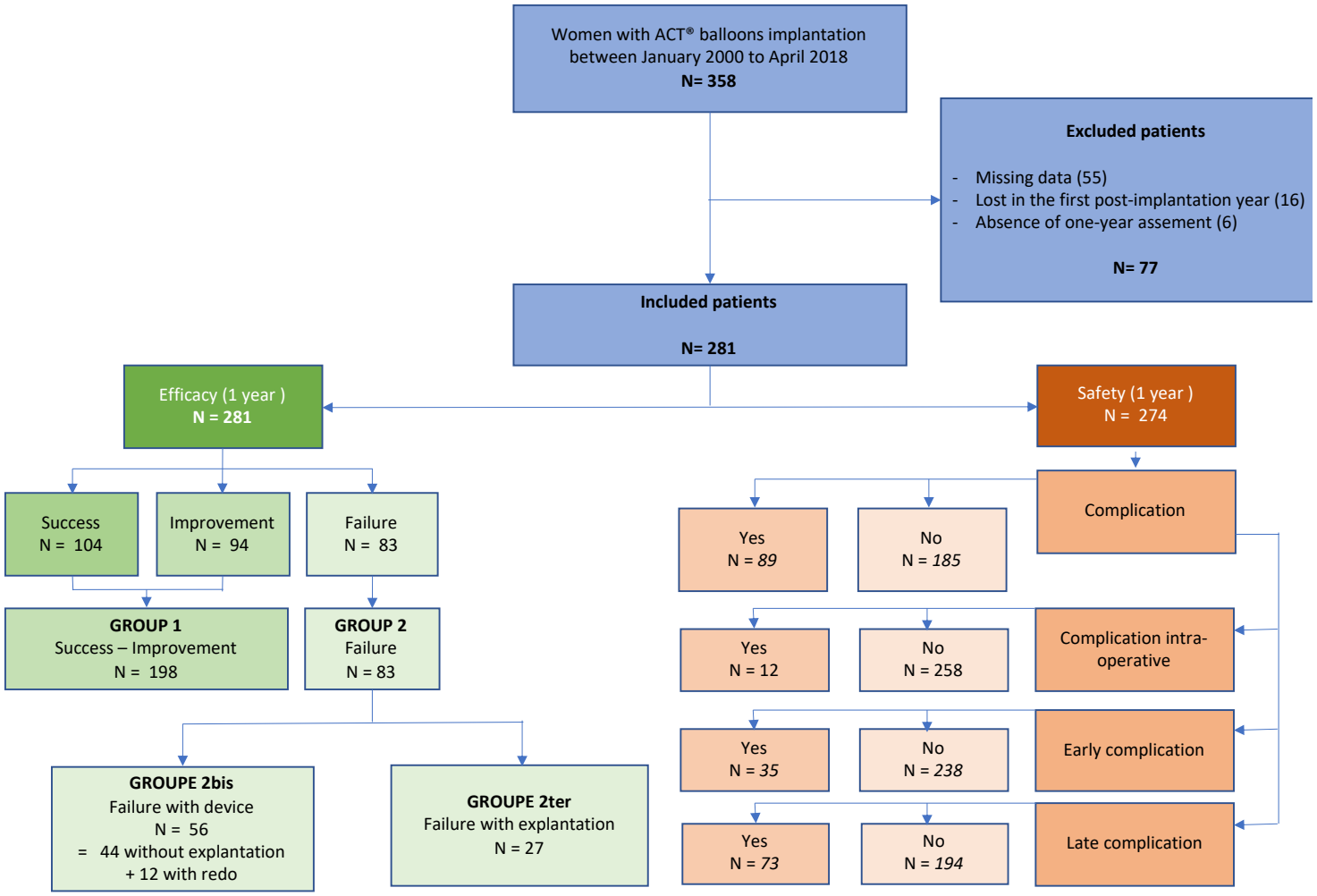
Table I : Patients characteristics

N excluded= 77 N included = 281	Standardized Difference
Age	<0.1
BMI (kg/m^2)	<0.1
Urinary incontinence	
Pure stress urinary incontinence	<0.1
Mixed urinary incontinence	
Daily pad use	<0.1
OAB therapy	
History of OAB therapy	<0.1
On-going OAB therapy	<0.2
Vaginal prolapse	
Overall	<0.5
Medical history	
Diabetes	<0.2
Underlying neurologic disease	<0.1
Pelvic radiation therapy	<0.2
Surgical history	
Stress urinary incontinence surgery	<0.1
Retro-pubic sub-urethral tape	<0.1
Trans-obturator sub-urethral tape	<0.2
Colposuspension	<0.2
Urethral bulking agents	<0.2
Artificial urinary sphincter	<0.2
Others	<0.2
Vaginal prolapse surgery (n,%)	<0.5
Obstetrical history	
Parity	<0.2
Vaginal delivery	<0.2
Urodynamic parameters	
Detrusor overactivity (n,%)	<0.2
Bladder compliance disorder (n,%)	<0.2
Qmax (mL/sec) (mean ± sd)	<0.5
PVR (mL) (mean ± sd)	<0.5
MUCP (mean ± sd)	<0.2

BMI : Body mass index ; OAB: OverActive Bladder ; Qmax : maximal uroflow ; PVR : Post-void residual volume ; MUCP : Maximal urethral closure pressure.

Table V : Standardized difference for baseline data between included and excluded women

Flow chart


Women with ACT® balloons implantation between January 2000 to April 2018
N= 358
Excluded patients
- Missing data (55)
- Lost in the first post-implantation year (16)
- Absence of one-year assement (6)
N= 77
Included patients
N= 281
Efficacy (1 year)
N = 281
Safety (1 year)
N = 274
Success
N = 104
Improvement
N = 94
Failure
N = 83
GROUP 1
Success – Improvement
N = 198
GROUP 2
Failure
N = 83
GROUPE 2bis
Failure with device
N = 56
= 44 without explantation
+ 12 with redo
GROUPE 2ter
Failure with explantation
N = 27
Complication
Yes
N = 89
No
N = 185
Complication intra-operative
Yes
N = 12
No
N = 258
Early complication
Yes
N = 35
No
N = 238
Late complication
Yes
N = 73
No
N = 194

Primary endpoint

One year after implantation, 104 women (37.0%) reported success, 94 women (33.5%) reported improvement, while 83 women (29.5%) reported failure. Overall, patients had a median daily pad use of 1.0 (1.0 ; 3.0) and a median NRS rated at 7/10 (4.0 ; 8.0). In the failure group, during this one-year follow-up, 27 women (36%) underwent a uni- or bilateral explantation without any redo procedure. Considering all groups, among the 38 women that underwent a redo procedure, 16 women (42.1%) and 10 women (26.3%) finally recovered success and improvement, respectively.

Secondary endpoints

Safety

An intra-operative complication occurred in 13 women (4.8%) while early and late post-operative complications were reported in 35 women (12.8%) and 73 women (27.3%),respectively.
Among the women that presented with a post-operative complication, 67 women (75.3%) underwent a uni- or bilateral explantation. Complications are summarized in Table II.

Risk factors for failure and complications

None of the peri-operative parameters assessed through a univariate analysis, were statistically associated with failure (Table III) or the occurrence of a post-operative surgical complication (Table IV).

		N = 281	
Overall surgical complications		99/274	36.1%
Post-operative surgical complications		89/274	32.5%
Intra-operative surgical complications			
Overall (n,%)		13/270	4.8%
Vaginal injury (n,%)		6/270	2.2%
Bladder injury (n,%)		4/270	1.5%
Urethral injury (n,%)		2/270	0.7%
Other (n,%)		1/270	0.4%
Early post-operative surgical complications			
Overall (n,%)		35/273	12.8%
Infection (n,%)		8/272	2.9%
Hematoma (n,%)		14/272	5.1%
Vaginal erosion (n,%)		2/271	0.7%
Bladder erosion (n,%)		1/271	0.4%
Urethral erosion (n,%)		0/271	0%
Other (n,%)		16/272	5.9%
Explantation (n,%)		9/270	3.4%
Late post-operative surgical complications			
Overall (n,%)		73/267	27.3%
Vaginal erosion (n,%)		19/265	7.2%
Bladder erosion (n,%)		4/265	1.5%
Urethral erosion (n,%)		9/265	3.4%
Other (n,%)		40/265	15.1%
Explantation(n,%)		62/266	23.3%
Explantations and Re-do procedures			
Explantation (n,%)		75/281	26.7%
	Unilatéral	41/281	14.6%
	Bilatéral	34/281	12.1%
Re-do procedure (n,%)		38/279	13.6%
	Unilatéral	28/279	10.0%
	Bilatéral	10/279	3.6%

Table II : Safety

	Success and Improvement N =198		Failure N=83		p-value
Age (median, IQR)	72.0	(61.0 ; 77.0)	69.0	(61.0 ; 77.0)	0.57
BMI (kg/m²) (median, IQR)	26.0	(22.9 ; 30.7)	27.1	(23.4 ; 30.5)	0.33
Urinary incontinence					
Pure stress urinary incontinence (n,%)	97	54.5%	33	43.4%	0.11
Mixed urinary incontinence (n,%)	81	45.5%	43	56.6%	
Daily pad use (median, IQR)	5.0	(3.0 ; 6.0)	5.0	(3.0 ; 6.0)	0.50
OAB therapy					
On-going therapy at baseline (n,%)	32	21.9%	17	32.1%	0.14
On-going therapy after a one-year (n,%)	29	17.1%	19	26.8%	0.086
Vaginal prolapse					
Overall (n,%)	19	14.8%	7	14.9%	0.99
Medical history					
Diabetes	25	13.3%	11	13.6%	0.95
Underlying neurologic disease (n,%)	36	18.6%	15	18.1%	0.92
Pelvic radiation therapy (n,%)	15	7.8%	7	8.4%	0.86
Surgical history					
Stress urinary incontinence surgery (n,%)	129	66.5%	50	60.2%	0.32
Vaginal prolapse surgery (n,%)	64	33.3%	22	26.5%	0.26
Other pelvic surgery (n,%)	88	51.8%	40	54.1%	0.74
Obstetrical history					
Parity (median, IQR)	2.0	(2.0 ; 3.0)	2.0	(2.0 ; 3.0)	0.99
Vaginal delivery (median, IQR)	2.0	(1.0 ; 3.0)	2.0	(1.0 ; 3.0)	0.93
Urodynamic parameters					
Detrusor overactivity (n,%)	28	17.7%	10	13.3%	0.40
Bladder compliance disorder (n,%)	7	5.6%	1	1.6%	0.27
MUCP (cmH_2O) (mean ± sd)	25.9	± 12.1	24.0	± 11.4	0.31
Intra-operative data					
Intra- operative complication	10	5.3%	3	3.8%	0.76
Vaginal injury	4	2.1%	2	2.5%	NA
Bladder injury	3	1.6%	1	1.3%	NA
Urethra injury	2	1.1%	0	0%	NA

BMI : Body mass index ; MUCP : Maximal urethral closure pressure ; NA : Non applicable; IQR: interquartile range.

Table III : Risk factor for failure

	No post-operative surgical complication **N=185**		Post-operative surgical complication **N = 89**		p-value
Age (median, IQR)	72.0	(61.0 ; 77.0)	71.0	(61.0 ; 76.0)	0.95
BMI (kg/m^2) (median, IQR)	26.6	(23.4 ; 30.5)	26.0	(22.1 ; 30.9)	0.49
Medical history					
Diabetes	25	14.3%	11	12.6%	0.72
Underlying neurologic disease (n,%)	38	20.9%	12	13.6%	0.15
Pelvic radiation therapy (n,%)	14	7.7%	6	6.9%	0.81
Surgical history					
Stress urinary incontinence surgery (n,%)	120	65.9%	57	64.8%	0.85
Vaginal prolapse surgery (n,%)	56	30.8%	29	33.7%	0.63
Other pelvic surgery (n,%)	82	50.9%	41	53.9%	0.66
Obstetrical history					
Parity (median, IQR)	2.0	(2.0 ; 3.0)	2.0	(1.0 ; 3.0)	0.17
Vaginal delivery (median, IQR)	2.0	(1.0 ; 3.0)	2.0	(1.0 ; 3.0)	0.19
Operating data					
Intra-operative complication (n,%)	10	5.5%	3	3.4%	0.56

BMI : Body mass index ; IQR: interquartile range.

Table IV : Risk factor for surgical complication

DISCUSSION

In the present study, one year after ACT® balloons have been implanted to treat mixed or stress UI, 37% and 33.5% of women achieved success and improvement, respectively. Surgical complications were reported in 36.1% women, including 4.8% of intra-operative complications and 32.5% post-operative complications. Explantation was performed in 26.7%, with a redo procedure in 50.6% of them. After an homogeneous one-year follow-up, we did not retrieve any risk factor associated with short-term failure or complication.

In terms of efficacy, our results concord with those already observed in the most recent literature with success and overall improvement rates ranging from 15% to 44%, and 66% to 78.4%, respectively[12].
However, the risk factor assessment performed in our large female population seriously questions the risk factors previously described for ACT® balloons failure. These risk factors, such as severity of incontinence[16] and pelvic radiotherapy[17], have been reported from male or mixed population. In women, only obesity has been proposed as a risk factor for failure [18] . This assumption was more recently disproved by Vayleux et al. [14], reporting a similar success rate of ACT® balloons between obese and non-obese women. These results concord with a systematic review published by Osbourn et al.[19], focusing on obesity and female stress urinary incontinence. The authors concluded, among others, that success of stress urinary incontinence surgery in obese women was similar to non-obese patients.

In terms of safety, our results concord with those already observed. Within recent literature, intra-operative complications were reported, to occur in 3.7% to 4.5% of cases, while one-year post-operative complications were higher, including urethral erosion (2–15 %), cutaneous erosion of the port (3–7.5 %), balloon migration (6.5–17.5 %), device infection (0.6–8.9 %) and balloon dysfunction (0.6–6 %) [12].

Abosseif et al. reported a rate of reimplantation ranged to 50% , as in the present study[20,21]. Reimplantation does not interfere with functional results and 2/3 of patients regain full or improved continence.

Although some risk factors for complications have been regularly reported in the recent literature, none has emerged from our study. In fact, these risk factors, such as pelvic radiotherapy, have been extracted from male or mixed population, and have never been isolated from strict female populations. In men, pelvic radiotherapy is mostly performed to treat prostate cancer, while in women it is usually performed to treat cervical, endometrial or colo-rectal cancer. Given these distinct indications, irradiation protocols may significantly vary between men and women in terms of dose and target volume. Therefore, consequences on the peri-urethral environment may significantly differ, explaining that pelvic radiotherapy constitutes a proven risk factor for complications in men, while it is not in women.

EAU guidelines, focusing on surgical treatment of female urinary incontinence, position the ACT® balloons at the same level than AUS for women with complicated SUI. However they clearly present with distinct efficacy and safety profiles. Where ACT® balloons show limited efficacy compared with AUS, they also demonstrate a lower complication rate, including only minor surgical complications easily managed with explantation mostly performed in ambulatory surgery.

Although several risk factors for failure and complications have already been reported for AUS, no risk factor associated with ACT® balloons has been identified in women yet. The present study by confirming the absence of any risk factors for failure and surgical complications associated with, will participate to clarify the place ACT® balloons in the algorithms of female SUI treatment. It may therefore be advocated not to restrain their indication in women, and even promote their use when handling patients with risk factors for AUS implantation.

Even if statistically powerfull and optimized by a multicentric conception, our study presents with several limitations and weakness, including its retrospective design - leading to a recurrent lack of data - as well as a short follow-up duration. Furthermore, the composite endpoint used, including both objective and subjective evaluation, even if appropriate to evaluate functional surgery, is not validated yet. Therefore, we cannot draw any definitive conclusion and advocate for future large prospective trials to be set up. To note, a prospective comparison with AUS is currently on-going through a large French multicentric RCT, and will undoubtedly help the urological community to better position ACT® balloons in future women SUI algorithms.

CONCLUSION

No risk factor was identified to predict short-term failure or complications associated with ACT® balloons in women. Even if limited in efficacy, this mini-invasive device presents with an interesting risk/benefit balance with local complications easily managed. ACT® balloons may therefore not be restrained to a selected population, and could be safely proposed in all patients presenting with mixed or stress urinary incontinence, whatever there comorbidities and medical or surgical history. especially when intrinsic sphincter deficiency is the predominant mechanism.

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Date de soutenance : 10 Juin 2020

Titre de la thèse : BALLONS ACT® (ADJUSTABLE CONTINENCE THERAPY) ET INCONTINENCE URINAIRE DE LA FEMME : EFFICACITE, COMPLICATIONS, FACTEURS DE RISQUE D'ECHEC ET DE COMPLICATIONS.

Thèse - Médecine - Lille 2020

Cadre de classement : *UROLOGIE*

Mots-clés : Incontinence urinaire de la femme, insuffisance sphinctérienne, ballons ACT®, ballons latéro-urétraux, complications

INTRODUCTION

Évaluer l'efficacité et les complications chirurgicales des ballons latéro-urétraux ACT® (Adjustable Continence Therapy) dans la prise en charge de l'incontinence urinaire (IU) d'effort par insuffisance sphinctérienne chez la femme, et rechercher les facteurs de risque d'échec et de complications chirurgicales.

METHODES

Toutes les femmes ayant eu une implantation de ballons ACT® entre 2000 et 2018 au sein de 5 CHU Français étaient éligibles. L'efficacité et les complications chirurgicales péri-opératoires étaient évaluées à un an. Concernant l'efficacité, les patientes étaient réparties en 3 groupes distincts. Succès : 1 protection par jour et une évaluation de la satisfaction du patient selon une échelle verbale simple (EVS) ≥ 8/10 ; Amélioration : diminution des protections par jour et EVS ≥ 5/10 ; Échec - stabilité ou augmentation des protections par jour ou EVS < 5/10. Dans un second temps, les facteurs de risque d'échec et de complications étaient recherchés.

RESULTATS

Parmi les 281 patientes inclues, 104 (37.0%) présentaient un succès alors que 83 (29.5%) étaient en échec. Au cours de l'année suivant l'implantation, une complication per- et/ou post-opératoire était rapportée chez 99 patientes (36.1%), et 75 patientes (26.7%) ont été explantées (uni ou bilatérale). Aucun complication majeure n'a cependant été rapportée. Aucun des facteurs de risques étudiés n'était statistiquement associé à l'échec ou à la survenue d'une complication chirurgicale post-opératoire.

DISCUSSION

Aucun facteur de risque d'échec ou de complication post-opératoire des ballons ACT® chez la femme n'a pu être identifié. Malgré son efficacité limitée, cette technique mini-invasive a une bonne balance bénéfice/risque avec des complications locales facilement prises en charge. Les ballons ACT® ne devraient pas être réservés à une population restreinte, mais pourraient être proposés à toutes les patientes présentant une IU d'effort ou mixte avec insuffisance sphinctérienne, quelques soient leurs comorbidités ou antécédent médical et chirurgical.

<u>Composition du Jury</u> :

Président : Monsieur le Professeur Arnauld VILLERS

Assesseurs : Monsieur le Professeur Michel COSSON

Monsieur le Professeur Xavier GAME

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