Age-stratified continence outcomes of robotic-assisted radical prostatectomy

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Introduction: *Incontinence after robot-assisted radical prostatectomy (RARP) significantly impacts quality of life. This study aims to compare the age-stratified continence outcomes in Canadian men undergoing RARP.*

Materials and methods: *A retrospective review was performed on a prospectively maintained database of 1737 patients who underwent RARP for localized prostate cancer between 2007 and 2019. Patients were stratified into five groups based on age: group 1, ≤ 54 years (n = 245); group 2, 55-59 years (n = 302) ; group 3, 60-64 years (n = 386); group 4, 65-69 years (n = 348); and group 5, ≥ 70 years (n = 116). Functional outcomes were assessed up to 36 months. Log-rank and multivariable Cox regression analyses were performed to compare the time to recovery of pad-free continence by age group.*

Results: *Continence rates of groups 1 to 5 were respectively 90.2%, 79.1%, 80.4%, 71.4%, and 59.8% at 1-year follow up ($p < 0.001$). After 3 years, groups 1 through 5 had continence rates of 97%, 91.7%, 89.3%, 81.4%, and 77.6%, respectively ($p < 0.001$). Median time to recovery of continence was 58, 135, 140, 152 and 228 days, respectively. Among men who remained incontinent, older patients consistently required more pads. In Cox proportional hazard model, groups 2, 3, 4 and 5 were respectively 33% ($p < 0.001$), 34% ($p < 0.001$), 33% ($p = 0.001$), and 41% ($p = 0.005$) more likely to remain incontinent compared to group 1.*

Conclusions: *Age is associated with significantly lower rates of continence recovery, longer time to recovery of continence, and more severe cases of incontinence after RARP.*

Key Words: robotic-assisted radical prostatectomy, RARP, continence, age, pads

Introduction

Over the past decade, robot-assisted radical prostatectomy (RARP) has become the procedure of choice for the treatment of locally advanced prostate cancer in most large urological centers of excellence. However, the rate of postoperative urinary incontinence (UI) remains a concern. Postoperative incontinence after RARP is an important part of patient counseling, as it is associated with decreased quality of life (QoL).[1] QoL impacts associated with UI may manifest themselves through preoccupation with leakage particularly through avoidant behaviors, a sense of helplessness, embarrassment and/or decreased hygiene. However, the data on age-stratified continence outcomes in patients undergoing RARP is scarce.[2]

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In our previous study, we compared the preoperative and postoperative functional outcomes in Canadian elderly patients who underwent RARP. We concluded that patients ≥ 70 years old undergoing RARP had significantly higher rates of incontinence postoperatively compared to patients aged 66-70 years old.[3] Other studies, such as the one by Kumar et al, showed similar results.[4] In this paper, we aimed to report age-stratified continence outcomes in Canadian men undergoing RARP in two high-volume academic centers between 2007 and 2019.

Material and methods

Between January 2007 and November 2019, 1737 men underwent RARP for localized prostate cancer at the Centre Hospitalier de l'Université de Montréal and Hôpital Sacré-Coeur de Montréal, two academic tertiary centers in Quebec, Canada. Inclusion criteria consisted of patients having at least 1 month of follow up after the procedure. A total of 1387 patients met the selection criteria all performed by a single, fellowship-trained surgeon. Patients were divided into five groups based on age: group 1, ≤ 54 years; group 2, 55-59 years; group 3, 60-64 years; group 4, 65-69 years; and group 5, ≥ 70 years.

Patient baseline characteristics were collected prospectively, including preoperative body mass index (BMI), transrectal ultrasound (TRUS) measurement of prostate volume, clinical staging, pathological evaluation (Gleason score), International Prostate Symptoms Score (IPSS) and Sexual Health Inventory for Men (SHIM) score. All patients had a serum prostate-specific antigen (PSA) drawn or proof of recent PSA value before surgery. Additional perioperative variables included operative time, final prostate specimen pathology, length of hospital stay, catheterization time, and incidence of blood transfusions. The postoperative clinical outcomes examined included IPSS, SHIM score, QoL score, and number of pads used. We recorded patients' data at each follow up visit (i.e. at 1, 3, 6, 9, 12, 18, 24, 30, 36 months postoperatively).

Functional outcomes

Functional outcomes were evaluated at baseline (preoperatively) and at each follow up visit. Lower urinary tract symptoms were evaluated using the self-administered IPSS questionnaire during clinic visits. Full continence was defined as a strict zero pad usage per day. QoL status was evaluated with a 0-6 scale answer to the question "If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?", 0 being the best score.

Surgical technique and pathological analysis

RARP surgical technique has been described in our prior reports.[5-7] Considering the modification of the Gleason grading system implemented during the previous years, RARP pathological specimens were analyzed by a team of three attending pathologists led by a dedicated genitourinary pathologist. Positive surgical margin (PSM) was defined as the presence of cancer at the inked margin.

Statistical analysis

Descriptive statistics were used to summarize our study population's baseline characteristics. Continuous variables were reported as median followed by the range as a measure of central tendency. All categorical variables were reported as proportions. Means of continuous variables were compared using an analysis of variance (ANOVA), while categorical variables were analyzed using the Chi-square test. Kaplan–Meier analysis was performed to compare the time to recovery of continence and differences between elderly age groups using log-rank testing. Cox proportional hazards regression models were used to evaluate the impact of time on continence by age group. Multivariable models were used and included age, BMI, PSA, preoperative IPSS and QoL score, TRUS and pathology measurement of prostate volume. A p value < 0.05 was considered statistically significant in all two-tailed tests. All statistical analyses were performed using RStudio Statistical package (Version 1.2.5033).

Results

Preoperative characteristics

A total of 1397 men were included for analysis. Groups 1, 2, 3, 4 and 5 comprised of 245, 302, 386, 348 and 116 men, respectively. Table 1 describes baseline patient characteristics. BMI was similar across all groups (p = 0.594). At baseline, there was a significant difference in preoperative PSA (p = 0.008) with men over 70 years of age having the highest mean PSA (7.8 ng/dL) and men in group 1 having the lowest mean PSA (5.7, SD = 4.9). Prostate volume, measured using TRUS, was significantly different between the groups and increased with age (p < 0.001).

With regards to preoperative urinary functions, IPSS and QoL score generally increased with age (p = 0.004 and p = 0.008, respectively), with group 1 patients demonstrating a lower IPSS score compared with group 5 (6.9 [SD = 6.0] and 10.5 [SD = 8.3], respectively) (QoL score 1.38 [SD = 1.46] and 1.93 [SD = 1.50], respectively). Biopsy Gleason score increased with

TABLE 1. **Patient baseline characteristics by age group**

	Group 1	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**p value**
Age group, years (n)	< 55 (245)	55-59 (302)	60-64 (386)	65-69 (348)	≥ 70 (116)	
Mean age, years (SD)	51.1 (3.0)	57.0 (1.4)	61.9 (1.4)	66.7 (1.4)	71.2 (1.4)	
Mean BMI, kg/m^2 (SD)	27.7 (4.3)	27.6 (4.5)	27.4 (4.1)	27.2 (4.1)	27.1 (5.0)	0.594
BMI groups % (n)						
< 30	77.1 (178)	76.9 (216)	80.3 (278)	80.4 (255)	81.3 (87)	0.322
≥ 30	22.9 (53)	23.1 (65)	19.7 (68)	19.6 (62)	18.7 (20)	0.214
Mean preoperative PSA, ng/dL (SD)	5.7 (4.9)	6.3 (3.5)	7.2 (4.1)	6.9 (3.4)	7.8 (6.9)	0.008
Mean TRUS prostate size, g (SD)	33.7 (13.3)	37.9 (16.1)	42.5 (19.1)	43.8 (20.0)	49.7 (27.2)	< 0.001
Mean specimen prostate size, g (SD)	44.6 (12.7)	48.2 (16.9)	52.9 (19.0)	56.1 (21.9)	63.2 (27.0)	< 0.001
D'Amico risk group, % (n)						< 0.001
Low	38.8 (93)	27.4 (81)	21.3 (80)	17.5 (59)	7.9 (9)	
Intermediate	55.0 (132)	64.9 (192)	67.6 (254)	65.4 (221)	72.8 (83)	
High	6.3 (15)	7.8 (23)	11.2 (42)	17.2 (58)	19.3 (22)	
Biopsy Gleason score, % (n)						< 0.001
6	43.9 (107)	29.8 (90)	25.7 (99)	21.6 (75)	9.6 (11)	
7	52.5 (128)	63.6 (192)	65.7 (253)	61.7 (214)	75.7 (87)	
≥ 8	3.7 (9)	6.6 (20)	8.6 (33)	16.7 (58)	14.8 (17)	
Specimen Gleason score, % (n)						< 0.001
6	23.4 (57)	16.6 (50)	14.8 (57)	7.8 (27)	7.8 (9)	
7	71.7 (175)	77.2 (233)	75.3 (290)	75.6 (263)	76.7 (89)	
≥ 8	4.9 (12)	6.3 (19)	9.9 (38)	16.7 (58)	15.5 (18)	
Clinical stage, % (n)						1.000
≤ T1c	79.8 (193)	77.1 (232)	78.0 (297)	71.2 (247)	67.8 (78)	
T2a	14.5 (35)	16.6 (50)	16.5 (63)	21.6 (75)	20.9 (24)	
T2b	3.7 (9)	4.7 (14)	3.9 (15)	4.6 (16)	9.6 (11)	
T2c	1.2 (3)	0.7 (2)	1.0 (4)	1.4 (5)	1.7 (2)	
T3	0.8 (2)	1.0 (3)	0.5 (2)	1.2 (4)	0	
Pathologic stage, % (n)						0.412
T2a	8.6 (21)	8.6 (26)	9.1 (35)	5.5 (19)	5.3 (6)	
T2b	5.3 (13)	6.6 (20)	4.9 (19)	4.6 (16)	3.5 (4)	
T2c	56.8 (138)	51.8 (156)	46.4 (179)	50.6 (175)	42.1 (48)	
T3a	24.7 (60)	27.9 (84)	32.6 (126)	31.5 (109)	43.9 (50)	
T3b	4.5 (11)	5.0 (15)	7.0 (27)	7.8 (27)	5.3 (6)	
Mean preoperative IPSS (SD)	6.9 (6.0)	7.0 (6.2)	8.3 (6.8)	8.7 (7.3)	10.5 (8.3)	0.004
Preoperative IPSS groups, % (n)						
0-7	63.6 (152)	63.2 (187)	56.1 (208)	54.2 (179)	45.5 (51)	0.0539
8-19	33.1 (79)	31.8 (94)	36.7 (136)	36.7 (121)	41.1 (46)	0.304
20-35	3.3 (8)	5.1 (15)	7.3 (27)	9.1 (30)	13.4 (15)	0.508
Mean preoperative SHIM (SD)	21.8 (4.7)	20.8 (5.3)	18.9 (6.4)	16.2 (7.0)	15.8 (7.3)	< 0.001
Preoperative SHIM, % (n)						
Potent (SHIM ≥ 17)	87.8 (208)	83.9 (245)	73.0 (265)	58.2 (189)	57.1 (64)	< 0.001
Impotent (SHIM < 17)	12.2 (29)	16.1 (47)	27.0 (98)	41.8 (136)	42.9 (48)	0.080
Preoperative QoL, mean (SD)	1.4 (1.5)	1.5 (1.5)	1.6 (1.4)	1.7 (1.5)	1.9 (1.5)	0.008
Preoperative QoL groups % (n)						
0-2	80.2 (182)	73.9 (212)	75.4 (264)	75.7 (243)	71.3 (77)	0.016
3-4	15.0 (34)	20.9 (60)	20.3 (71)	19.0 (61)	21.3 (23)	0.186
5-6	4.8 (11)	5.2 (15)	4.3 (15)	5.3 (17)	7.4 (8)	0.056

BMI = body mass index; PSA = prostate-specific antigen; TRUS = transrectal ultrasound; IPSS = International Prostate Symptoms Score; SHIM = Sexual Health Inventory for Men; QoL = quality of life

TABLE 2. **Perioperative outcomes by age group**

	Group 1	Group 2	Group 3	Group 4	Group 5	p value
Age group, years (n)	< 55 (245)	55-59 (302)	60-64 (386)	65-69 (348)	≥ 70 (116)	
Mean estimated blood loss, mL^3 (SD)	234.2 (148.5)	251.6 (135.7)	250 (134.7)	271 (166.7)	275.1 (183.1)	0.025
Mean foley removal day, days (SD)	5.6 (1.5)	6.0 (2.3)	6.0 (1.9)	6.2 (2.7)	5.9 (1.8)	0.021
Mean operative time, minutes (SD)	170.2 (45.9)	175.2 (47.8)	170 (48.0)	184.4 (53.3)	177.5 (40.6)	0.011
Nerve sparing rate, % (n)						< 0.001
Unilateral	12.9 (31)	19.5 (58)	16.1 (60)	19.0 (64)	13.2 (15)	
Bilateral	73.3 (176)	58.7 (175)	55.6 (207)	41.7 (140)	35.1 (40)	
Non-nerve sparing	13.8 (33)	22.0 (65)	28.2 (105)	39.3 (132)	51.8 (59)	
Clavien-Dindo complication rate, % (n)						< 0.001
No complications	138	162	386	348	116	
1	74	109	129	142	41	
2	24	20	35	33	8	
3a	6	6	3	5	2	
3b	3	4	1	5	0	
4a	0	0	1	3	1	
4b	0	1	0	0	0	

age, with over 91.5% of group 5 patients presenting with a Gleason score of 7 and above, compared to only 61.3% in group 1 (p < 0.001).

Perioperative outcomes

Table 2 summarizes all groups perioperative outcomes. Estimated blood loss varied significantly across age groups (p = 0.025). Furthermore, length of operation and catheterization were statistically different between groups (p = 0.011 and p = 0.021, respectively), and also generally increased with age. There were significant differences across groups in the incidence of nerve-sparing procedures (p < 0.01), with group 5 having the highest proportion of patients undergoing a non-nerve sparing surgery (51.8%), and group 1 having the highest proportion of patients undergoing a bilateral nerve-sparing procedure (73.3%).

3-year outcomes

Figure 1 demonstrates the age-specific outcomes of RARP over a 3-year follow up. There was a statistically significant difference in mean postoperative IPSS score at 3, 6, 9, and 12 months, with group 5 patients demonstrating the highest IPSS scores. The mean IPSS change from baseline was significantly different across groups at all time points after the 1-month follow up, with group 5 consistently displaying the highest decrease in IPSS. In terms of QoL score, despite the generally higher values found for group 5, a statistically significant difference in mean QoL score was only seen at 6- and 12-month follow up. Furthermore, the mean QoL score change from baseline was significantly different in all groups at every follow up period.

Continence

Older men consistently demonstrated less favorable continence outcomes. Figure 2 demonstrates continence rate with respect to time after surgery. Patients in groups 1 through 3 obtained 90.2%, 79.1%, and 80.4% strict 0-pad continence at 1-year follow up, respectively. On the other hand, groups 4 and 5 obtained 71.4% and 59.8% continence rates at the same time point, respectively. The median time to recovery of continence was 58, 135, 140, 152 and 228 days for groups 1 through 5, respectively. After 3 years, 97% of patients in group 1, 91.7% of patients in group 2, 89.3% of group 3, 81.4% of group 4, and 77.6% of group 5 were fully continent.

Furthermore, among postoperative incontinent patients, the severity of incontinence varied significantly between the age groups. Figure 1G demonstrates the mean number of pads used per day amongst incontinent patients in each age group. The number of pads used varied significantly between the groups with the oldest age group generally using a higher mean number of pads per day. At 1 month, the mean number of pads in group 1 through 5 (0.80,

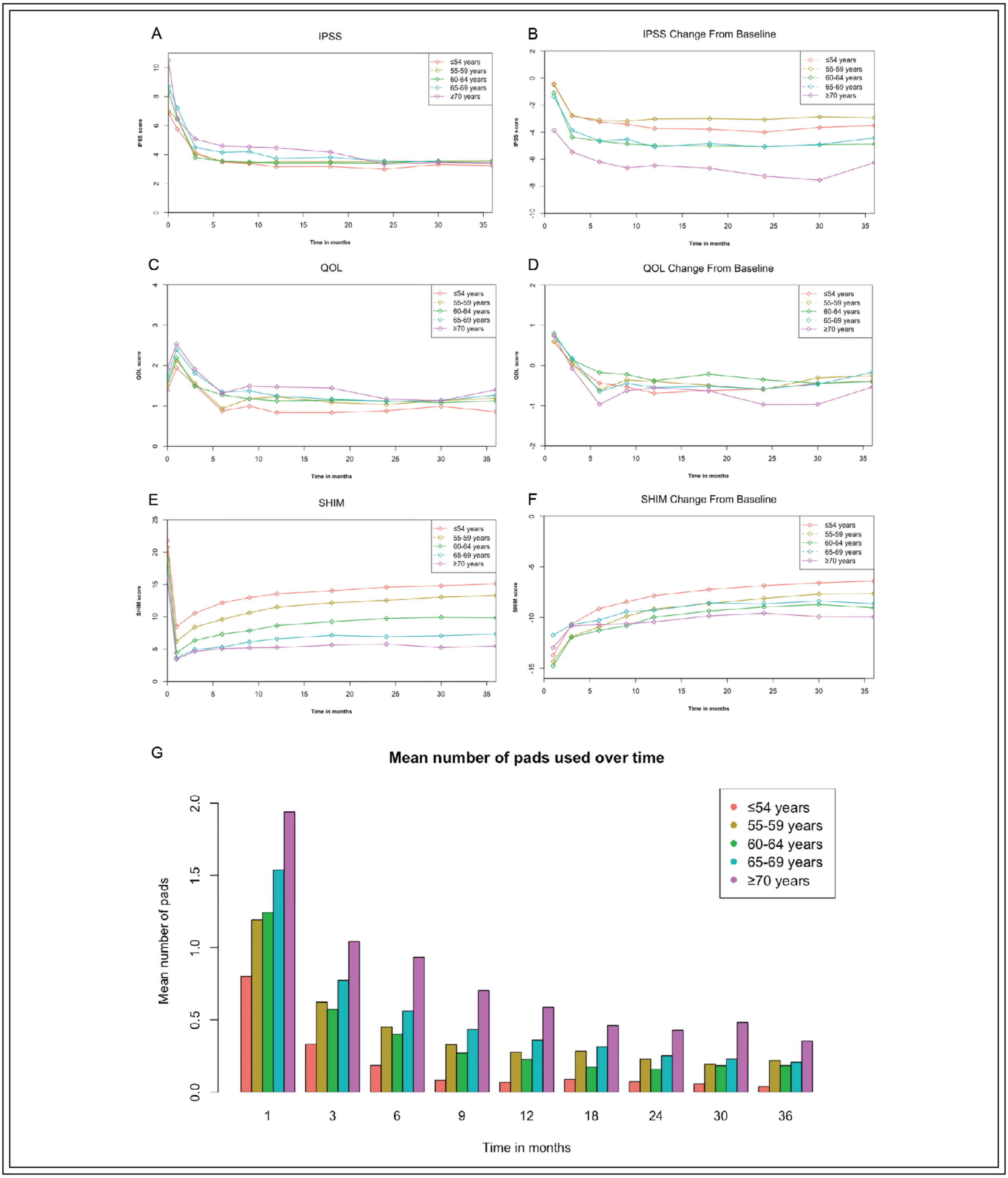

Figure 1. Age-specific outcomes over time. **(A)** Mean IPSS score over time **(B)** Mean IPSS change from baseline over time **(C)** Mean QoL score over time **(D)** Mean QoL score change from baseline over time **(E)** Mean SHIM score over time **(F)** Mean SHIM score change from baseline over time **(G)** Mean number of pads used over time in patients who were still incontinent in each age group.

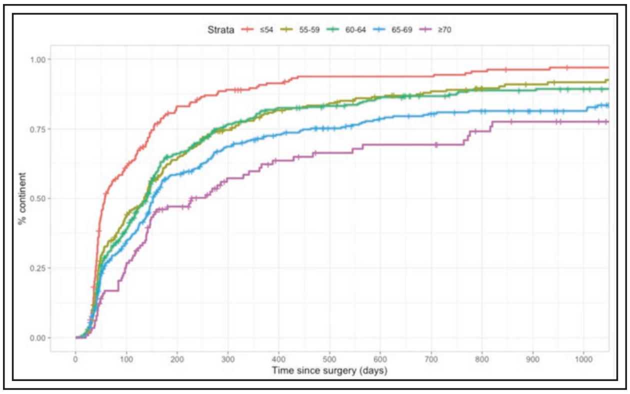

Figure 2. Age-specific continence recovery of all patients after surgery.

1.19, 1.24, 1.54 and 1.94 respectively, $p < 0.001$) was expectedly lower than at 36 months (0.04, 0.22, 0.18, 0.21, 0.35 respectively, $p < 0.001$). Difference in mean number of pads used between groups remained statistically significant throughout the study.

Multivariable cox proportional hazard model

On multivariable analysis, groups 2, 3, 4 and 5 were respectively 33% [hazard ratio (HR) 0.67; 95% CI (0.55, 0.83); $p < 0.001$], 34% [HR 0.66; 95% CI (0.53, 0.82); $p < 0.001$], 33% [HR 0.67; 95% CI (0.53, 0.86); $p = 0.001$], and 41% [HR 0.59; 95% CI (0.41, 0.85); $p = 0.005$] less likely to fully return to continence per unit of time compared to patients in group 1. BMI, TRUS calculated prostate volume, preoperative PSA, preoperative IPSS score, preoperative QoL score, and duration of hospitalization were not statistically significant risk factors for postoperative incontinence. On further analysis, there were no significant differences on multivariable analysis between patients with different cancer risk group (Gleason 7 versus Gleason 8-10).

Discussion

Curative therapies for localized prostate cancer are performed for clinically significant prostate cancer for a wide age range of patients. However, RARP has documented operative complications which can significantly impact a patient's QoL.[8-10] Incontinence is a common complication of this procedure and plays an important role in the postoperative QoL. Penson et al found that urinary function post-RP is the strongest predictor of patient health-related quality of life (HRQoL), when compared to other factors such as treatment modality and postoperative sexual function.[11] Depending on patient age, the level of concern with a specific complication varies significantly. For instance, the risk of impotence causes greater anxiety for younger patients.[12] Previous studies have demonstrated that the QoL and functional outcomes of RARP vary significantly based on a patient's age.[3,4] Therefore, age stratified RARP outcomes are beneficial to urologists during preoperative counseling and may allow further decision individualization. In this paper, we aimed to assess the age-related functional and continence outcomes of RARP across five different age groups. We were able to describe an age-related increase in rates and severity of incontinence, and median time to continence recovery.

Counseling patients on realistic expectations in terms of continence is challenging, given the lack of age-stratified studies. The lack of a standardized definition of continence in the literature also makes it challenging to accurately define outcomes. Liss et al compared urinary QoL scores between men with no post-radical prostatectomy pads use (strict 0-pads definition of continence), and men using security pads, 0 or 1 pads.[13] The men within the strict 0-pad group were found to have significantly better QoL scores when compared to the 3 other patients' groups. Thus, our study has defined continence as a strict 0-pads use.

In the current study, over 90% of men younger than 60 years and over 80% of men aged 60-69 years achieved strict pad free continence after 36 months. In comparison, only 77.6% of men over the age of 70 regained continence 3 years after surgery. The rates of continence of the oldest age group remained consistently lower than groups 1-4 across all time points. Several factors may explain the age-related discrepancies in recovery of continence. Intraoperatively, RARP can cause damage to the sphincteric mechanism and the surrounding supporting structures of the pelvis (ligaments, tendineus fascia, endopelvic fascia, Denonviller's fascia and detrusor slips).[14] It is known that continence is generally controlled by a combination of the action of the detrusor muscle, the proximal intrinsic sphincter, the rhabdosphincter and the supporting structures.[14,15] Thus intraoperative damage to these structures might have impacts in the postoperative continence status of the patient.

It is also known that older patients have decreased lean body mass and skeletal muscle function. Furthermore, the simple accumulation of age-related microvascular disease and decreased blood flow to wound sites can impair wound healing and inflammatory responses.[16-18] Finally, an age-related decrease in neuronal plasticity can hinder the ability of pelvic floor muscle adaptation after surgery in older men.[19] These factors can affect postoperative healing and contribute to worse continence recovery in the aging male.

Mendiola et al evaluated the age-stratified continence outcomes of 338 consecutive patients who underwent RARP.[20] Their findings showed similar 1-year continence outcomes between men of different age groups, also suggesting that younger men achieved subjective continence significantly earlier than older men. Kumar et al performed an age-stratified, propensity score matched study looking at age-related outcomes after RARP.[4] They found a similar 24-month follow up continence rate for patients under and over 70 years of age (91.3% and 87.3%, respectively; p = 0.06).

Although the relationship between nerve-sparing surgery and continence is not well understood, a meta-analysis performed by Reeves et al demonstrated that nerve-sparing surgery results in faster return of continence in the 6 months following the surgery.[21] However, there is no evidence showing differences in long term continence rates between nerve-sparing and non-sparing RARP patients. In our study, we looked at long term continence outcomes, both non-nerve sparing and nerve-sparing patients were included.

Unique to our study, we also looked deeper into the level of incontinence rather than a binary outcome. The severity of incontinence, measured in this study using a daily number of pads, was generally higher in older age groups and remained significantly different throughout the 3-year follow up. Basto et al measured the number of pads used per day in patients after RARP, with stratification based on age.[22] They were able to appreciate a significant difference in the number of pads used at 4-6 week follow up (1.1 pads per day in patients < 70 years old and 1.9 pads in patients > 70 years old, p = 0.034). At 3, 6, 9, and 12-month after surgery, the difference in number of pads was no longer appreciated. However, the study displayed a low sample size of 24 patients over the age of 70. Patients who were deemed continent were also included in their calculation. In our sub-analysis, we excluded patients who had recovered continence in order to further isolate and describe the severity of age-related incontinence after RARP in those who were still incontinent.

On multivariate analysis, age was the only covariate significantly associated with increased risk of incontinence in all age groups. Neumaier et al performed a multivariate analysis on 104 consecutive RARP patients looking for factors associated with continence recovery. They found that, when examined as a continuous variable, age was not associated with continence recovery in univariate analysis.[23] However, when age was analyzed as a categorical variable (i.e. ≤ 60 years and > 60 years), it was a significant predictor of continence recovery (p = 0.03). Like our results, their study also did not find any significant change in continence rates based on BMI, PSA, prostate volume and D'Amico risk score.

Our study was able to show an association between age of patients and the continence of patients after RARP. Younger patients show better continence outcomes than their older counterparts. However, older patients had relatively good rates of continence recovery and the pads use significantly decreased with time. Yet, there is multiple limitations to consider. A major limitation of this study pertains to its retrospective design. The older patients in our study also represent a highly selected cohort who were likely healthier and highly motivated to undergo the operation. Furthermore, these patients underwent non-nerve sparing procedures at a higher rate than younger groups, which can impact short term continence outcomes. Data from our study represent the outcomes of RARP performed by a single surgeon in a high-volume center and may therefore not be generalizable to all surgeons and all centers. Despite these limitations, the strengths of our study include a long follow up time, a large sample size and a strict definition of continence. This is the first Canadian study to assess RARP continence outcomes according to age.

Conclusion

This study demonstrates that RARP has good functional outcomes as a definitive treatment for prostate cancer, regardless of age. However, older men had inferior continence recovery rates, longer time to recovery of continence, and more severe incontinence compared to younger patients. Such data is valuable in prognostic evaluation, counseling, and realistic patient expectations. □

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