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Assessing pentafecta achievement after robot-assisted radical cystectomy and its association with surgical experience: Results from a high-volume institution

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Abstract

Objectives: Radical cystectomy (RC) represents the gold standard treatment for high-risk bladder cancer. Despite evidence suggesting that surgical experience correlates with perioperative and oncologic outcomes of robot-assisted RC (RARC), validated tools to assess its quality objectively are lacking. We aimed to evaluate the impact of RC-Pentafecta (absence of early major complications, absence of urinary diversion related sequelae at ≤12 months, absence of soft tissue surgical margins, ≥16 lymph nodes at final pathology and absence of clinical recurrence at ≤12 months) on oncological outcomes and the role of surgical experience on its achievement.

Materials and methods: We retrospectively evaluated 366 patients undergoing RARC with intracorporeal urinary diversion in a single tertiary centre with a minimum of 1 year follow-up. Surgeries were performed using the DaVinci Xi system according to a previously described technique. Kaplan-Meier curves were used to investigate 5-years overall survival and cancer specific mortality-free survival (CSS) according to RC-Pentafecta achievement. Multivariable Cox's regressions were performed to evaluate the impact of RC-Pentafecta on overall mortality. Multivariable logistic regressions were performed to explore the effect of surgical experience on RC-pentafecta achievement. Locally weighted scatterplot smoother function was used to graphically explore this relationship.

Results: Patients achieving RC-Pentafecta showed higher 5-year overall survival (71.8% vs. 59.6%, $P < 0.001$) and CSS (84% vs. 71%, $P < 0.001$) when compared with patients not achieving it. At multivariable Cox's regression, RC-Pentafecta achievement (HR 0.57, $P = 0.03$), positive surgical margins (HR 2.48, $P = 0.002$), pN+ (HR 2.23, $P = 0.002$), pT≥3 (HR 1.71, $P = 0.04$) and current smoking status (HR 2.4, $P = 0.006$) were significant predictors of overall mortality. At multivariable logistic regression surgical experience (OR 1.2, $P < 0.001$), age (OR 0.93, $P = 0.04$), previous prostate surgery (OR 0.7, $P = 0.02$) and pT≥3 (OR 0.8, $P = 0.03$) were independent predictors of

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RC-Pentafecta achievement. A linear relationship between surgical experience and RC-Pentafecta achievement, without reaching a plateau, was observed.

Conclusions: RC-Pentafecta is a valuable tool to assess surgical quality of RARC and the experience of the center where the surgery is performed and may be used to identify "referral" centers for treatment of high-risk bladder cancer.

Keywords: Complications; Cystectomy; Intracorporeal urinary diversion; Minimally invasive surgery; Oncologic outcomes; Pentafecta; Robot assisted cystectomy; Surgical experience

1. Introduction

Over the last 10 years, several strategies to improve radical cystectomy (RC) outcomes, such as enhanced recovery protocols and minimally invasive approaches [1], have been proposed. However, RC is still associated with high rates of postoperative adverse events [2] and mortality, regardless of the approach used [3]. Despite evidence suggesting that surgical experience correlates with the perioperative and oncologic outcomes of robot-assisted RC (RARC) [4], validated tools to assess RARC quality objectively are lacking. Cacciamani et al. proposed the RC-Pentafecta model aimed to standardize the reporting of optimal perioperative and oncologic outcomes [5]. This model included two indexes of perioperative morbidity, namely absence of early (≤90 days) major complications and absence of urinary diversion (UD) related sequelae at ≤12 months, and three surrogate indexes of oncological adequacy, namely absence of soft tissue surgical margins, ≥16 lymph nodes yielded at final pathology and absence of clinical recurrence at ≤12 months. This pentafecta was recently applied by Oh et al., showing a significant correlation between RC-Pentafecta achievement and survival outcomes in patients undergoing RARC [6]. However, the authors relied on a multi-institutional heterogeneous RARC series where 21 surgeons with different surgical experience were involved [6]. Moreover, the authors did not collect postoperative complications relying on the standardized methodology proposed by the European Association of Urology (EAU) [7]. Lastly, uretero-ileal strictures were used as the only parameter to define UD-related sequelae [8]. To overcome these issues, we aimed to evaluate the impact of RC-Pentafecta on oncological outcomes and the role of surgical experience on RC-Pentafecta achievement, evaluating its parameters as suggested in the original article. For this, we relied on a large single center intracorporeal RARC series with a minimum of 1-year follow-up.

2. Material and methods

2.1. Study population

The current study relied on an institutional reviewed board-approved prospectively maintained database. It included 381 consecutive patients treated with RARC with intracorporeal UD (ICUD) for bladder cancer at a single high-volume centre (Onze-Lieve-Vrouwziekenhuis, Aalst, Belgium) from 2004 to 2020. Demographic characteristics at baseline, perioperative and pathological data, complications, and oncological outcomes were collected for all patients. Patients with a follow-up shorter than 12 months (n = 15) were excluded from the current analysis. This yielded a final population of 366 patients. This study was conducted in the accordance with good clinical practice guidelines and the ethical principles of the Declaration of Helsinki.

2.2. Surgical technique

All surgeries were performed by two surgeons (A.M. and F.D.) with extensive experience (>1000 procedures) in robotic surgery. Surgical procedures were performed according to a previously described technique [9–12]. The decision to perform ileal conduit (IC) or orthotopic neobladder (ONB) was based on established guidelines considering patients' and disease characteristics [13]. All patients were postoperatively managed according to enhanced recovery after surgery (ERAS) protocols [14].

2.3. Radical cystectomy pentafecta definition

RC-Pentafecta and its items, namely lymph nodes yielded at final pathology ≥16, absence of early (≤90 days) major complications [Clavien-Dindo (CD) ≥3a], absence of soft tissue margins (STM), absence of disease recurrence within 12 months from surgery, absence of UD-related sequelae within 12 months from surgery, were defined as described by Cacciamani et al. [5]. Patients who met all the five criteria were considered to have achieved RC-Pentafecta.

2.4. Outcomes

The primary outcome of the study was to evaluate the impact of RC-Pentafecta achievement on oncological outcomes, namely overall survival (OS) and cancer-specific mortality free-survival (CSS). To perform an accurate evaluation of RC-Pentafecta rates, a retrospective collection for overall early (≤90-days) postoperative complications was performed based on patient' charts and follow-up interviews by two medical doctors. Postoperative complications were defined according to the Common Terminology

Criteria for Adverse Events v.5.0 [15] and graded according to CD classification [16]. The reports of complications followed the quality criteria for accurate and comprehensive reporting of surgical outcomes recommended by the EAU Guidelines [7] (Supplementary Table 1). As secondary outcomes we assessed the impact of surgical experience on RC-Pentafecta achievement and RC-Pentafecta achievement rates according to UD type.

2.5. Statistical analyses

Statistical analyses, reporting, and interpretation of the results were conducted according to established guidelines [17]. Based on RC-Pentafecta achievement, patients were divided into two groups for analysis. Descriptive statistics included frequencies and proportions for categorical variables. Medians with interquartile ranges (IQR) were reported for continuously coded variables.

Six sets of analyses were performed. First, chi-square and Mann-Whitney U-tests were performed to examine the statistical significance in proportions' and medians' differences on the baseline and perioperative characteristics, as well as oncological outcomes according to RC-Pentafecta achievement.

Second, Kaplan-Meier plot was used to investigate 5-years OS and CSS according to RC-Pentafecta achievement. Multivariable Cox proportional hazard regressions were performed to evaluate the impact of RC-Pentafecta achievement on overall mortality (OM). Adjustment variables consisted of age, gender, Charlson Comorbidity Index (CCI), diabetes mellitus (DM), smoking status, neodjuvant chemoteraphy (NACH), UD type, pT and pN. Model's discrimination and calibration abilities were tested using Harrel's C-index and calibration plot, respectively. Third, sensitivity analysis according to ileal conduit urinary diversion was performed. Fourth, multivariable Cox proportional hazard regressions were performed to evaluate the impact of each item composing RC-Pentafecta on OM and CSS.

Fifth, multivariable logistic regression analyses were performed to explore the effect of surgical experience on RC-pentafecta achievement. Surgical experience was coded as the number of prior robotic cystectomies performed by each surgeon at the time of each patient's surgery [18]. Surgical experience was modeled, when significant, as a non-linear term using restricted cubic splines with four knots at quartiles. Statistical significance of cubic splines simultaneous was evaluated using the test for all spline terms [4]. Adjustment variables consisted of age, gender, CCI, body-mass index (BMI), previous prostate surgery, DM, smoking status, NACH, UD type, and pT stage.

Finally, a locally weighted scatterplot smoother (LOWESS) function was used to graphically explore the relationship between surgical experience and RC-Pentafecta achievement, after accounting for all aforementioned confounders [4]. All statistical analyses were performed using R studio graphical interface for R v.4.0.1. All tests were two-sided, with a level of significance set at $P < 0.05$.

3. Results

3.1. General characteristics of the study populations

Preoperative characteristics of the study population are reported in Table 1. Overall, 191 (52.2%) patients achieved RC-Pentafecta. Patients achieving RC-Pentafecta had a lower rate of previous prostatic surgery (7% vs. 26%, $P = 0.03$) when compared with those not achieving RC-Pentafecta. No statistically significant differences were recorded in terms of age at surgery, BMI, ASA score, CCI, DM, NACH, cT, and cN stage (all $P \geq 0.05$).

3.2. Perioperative outcomes

Table 2 illustrates perioperative outcomes according to RC-Pentafecta achievement. Patients achieving RC-Pentafecta had statistically significant lower estimated blood loss (300 vs. 350 ml, $P = 0.007$), shorter length of stay (11 vs. 13 days, $P < 0.001$), lower perioperative mortality (0% vs. 3.4%, $P < 0.001$), and a lower rate of overall 90-days complications (41% vs. 51%, $P < 0.001$) when compared with those not achieving RC-Pentafecta. Supplementary Table 2 illustrates early (≤90 days) postoperative complications collected according to the standardized criteria (Supplementary Table 1) recommended by EAU guidelines. Overall, 14/14 criteria were met. Rates of intraoperative complications, readmission rates, and operative time did not differ between the groups (all $P \geq 0.05$).

3.3. Pathological and oncological outcomes

Pathological features and oncological outcomes according to RC-Pentafecta achievement are summarized in Table 3. Overall, 131 (35.8%) had ≥ pathological T3 and 50 (14%) had pN+ diseases. Patients achieving RC-Pentafecta had lower rates of pT3 diseases (33% vs. 40%, $P = 0.04$) and experienced lower rates of overall surgical margins (1.5% vs. 14.1%, $P < 0.001$) when compared with those not achieving RC-Pentafecta. Overall, 29 (8%) patients experienced disease recurrence within 12 months from RC. Site of recurrence was local, upper urinary tract and distant site in 5 (1.3%), 2 (0.5%), and 22 (6.2%) patients, respectively. During a median follow-up of 29 months (IQR 14–55), patients achieving RC-Pentafecta experienced lower overall mortality (26% vs. 48%) and cancer-specific mortality free-survival (13% vs. 30%) compared with patients not achieving RC-Pentafecta. No differences were recorded between the two groups in terms of adjuvant chemotherapy (7.8% vs. 8%, $P = 0.8$) and salvage chemotherapy (12% vs. 17%, $P = 0.3$) administration. At survival analysis, patients in the RC-Pentafecta group showed higher 5-year OS (71.8% vs. 59.6%, $P < 0.001$,

Table 1
Overall demographics and clinical features of 366 patients treatet with robot-assisted RC.

Variables	Overall (n = 366)	RC-Pentafecta (n = 191)	No RC-Pentafecta (n = 175)	*P* value
Age (years)				
Median (IQR)	71 (63–78)	70 (62–77)	72 (63–78)	0.05
BMI (kg/m^2)				
Median (IQR)	26 (23–28)	25 (23–27)	27 (23–29)	0.08
Gender, n (%)				
Male	305 (83)	160 (84)	145 (83)	0.8
Female	61 (17)	31 (16)	30 (17)	
ASA score, n (%)				
II	211 (58)	114 (60)	97 (55)	0.2
III	151 (41)	76 (39)	75 (43)	
IV	4 (1)	1 (1)	3 (2)	
CCI				
Median (IQR)	4 (2–5)	4 (2–5)	4 (3–5)	0.2
Smoking status, n (%)				
Never	168 (46)	78 (41)	90 (51)	0.1
Current	140 (38)	78 (41)	62 (35)	
Former	58 (16)	35 (18)	23 (14)	
Diabetes, n (%)				
Yes	59 (16)	24 (13)	35 (20)	0.05
No	307 (84)	167 (87)	140 (80)	
Previous prostate surgery, n (%)[b]				
No	255 (84)	148 (93)	107 (74)	0.03[a]
RARP	40 (13)	10 (6)	30 (21)	
TURP/HoLEP	10 (3)	2 (1)	8 (5)	
NACH, n (%)				
Yes	93 (25)	50 (26)	43 (25)	0.7
No	273 (75)	141 (74)	132 (75)	
cT≤2, n (%)				
Yes	302 (82)	159 (83)	143 (81)	0.7
No	64 (18)	32 (17)	32 (19)	
cT, n (%)				
cTx	8 (2.2)	5 (2.6)	3 (1.7)	0.9
cTIS	16 (4.4)	10 (5.2)	6 (3.4)	
cTa	16 (4.4)	9 (4.6)	7 (4)	
cT1	59 (16)	33 (17.3)	26 (14.9)	
cT2a	202 (55.2)	102 (53.4)	100 (57)	
cT2b	1 (0.3)	0 (0)	1 (0.7)	
cT3a	3 (0.9)	2 (1)	1 (0.7)	
cT3b	44 (12)	21 (11)	23 (13)	
cT4a	17 (4.6)	9 (4.6)	8 (4.6)	
cN, n (%)				
cN0	310 (85)	162 (85)	148 (85)	0.6
cN1	32 (9)	16 (8)	16 (9)	
cN2	12 (3)	8 (4)	4 (2)	
cN3	12 (3)	5 (3)	7 (4)	

ASA = American society of Anesthesiologists; BMI = Body-mass index; CCI = Charlson Comorbidity Index; HoLEP = Holmium Laser Enucleation of Prostate; IQR = interquartile ranges; NACH = Neoadjuvant chemotherapy; RARP = Robot-assisted Radical Prostatectomy; RC = Radical Cystectomy; TURP = Transurethral Resection of Prostate.

[a] Statistically significant.

[b] Only male population.

Fig. 1A) and 5-year cancer-specific mortality free-survival (84% vs. 71%, $P < 0.001$, Fig. 1B) when compared with patients not achieving RC-Pentafecta. At multivariable Cox's proportional hazard regression model, RC-Pentafecta achievement (HR 0.53, $P = 0.03$), pN+ (HR 2.19, $P = 0.003$), pT≥3 (HR 1.74, $P = 0.04$), ONB (HR 0.48, $P = 0.001$) and current smoking status (HR 2.23, $P = 0.007$) were significant predictors of overall mortality (Fig. 2). The C-index of the model was 72% and the model showed a near perfect calibration (Fig. 3). Each item composing RC-Pentafecta had a significant impact on OM and CSS (Supplementary Table 3).

3.4. Sensitivity analysis

At multivariable Cox's proportional hazard regression model fitted including only patients undergoing RARC with ileal conduit, RC-Pentafecta achievement (HR 0.42,

Table 2
Perioperative outcomes of 366 patients treated with robot-assisted RC.

Variable	Overall (n = 366)	RC-Pentafecta (n = 191)	No RC-Pentafecta (n = 175)	*P* value
Type of UD, n (%)				
Neobladder	82 (22)	57 (30)	25 (14)	0.004[a]
Ileal conduit	284 (78)	134 (70)	150 (86)	
Operative time (min)				
Median (IQR)	347 (300−400)	335 (294−393)	355 (300−420)	0.1
EBLs (ml)				
Median (IQR)	300 (200−500)	300 (150−400)	350 (200−500)	0.007[a]
Intraoperative complications, n (%)	7 (1.9)	3 (1.5)	4 (2.2)	0.8
Perioperative transfusions, n (%)	20 (5)	7 (3)	13 (8)	0.1
Length of stay (d)				
Median (IQR)	12 (9−15)	11 (9−13)	13 (10−19)	<0.001[a]
Peri-operative mortality, n (%)	6 (1.6)	0 (0)	6 (3.4)	<0.001[a]
N. lymph nodes removed				
Median (IQR)	19 (15−22)	19 (19−24)	15 (13−19)	<0.001[a]
30 d complications, n (%)	115 (31.4)	59 (31)	56 (32)	0.2
CD 30 d complications, n (%)				
CD≤2	89 (24.3)	59 (31)	30 (17)	<0.001[a]
CD≥3	26 (7)	0 (0)	26 (15)	
90 d complications, n (%)	168 (46)	78 (41)	90 (51)	<0.001[a]
CD 90 d complications, n (%)				
CD≤2	124 (34)	78 (41)	46 (26)	<0.001[a]
CD≥3	44 (12)	0 (0)	44 (25)	
Readmission, n (%)	62 (16)	23 (12)	39 (22)	0.06
Readmission's causes, n (%)				
Small bowel obstruction	9 (14)	0 (0)	9 (23)	0.05
Fever of unknown origin	15 (24)	9 (39)	6 (15)	
Pyelonephritis	17 (27)	10 (44)	7 (19)	
Intra-abdominal abscess	3 (5)	0 (0)	3 (8)	
Urinary leak	8 (13)	0 (0)	8 (20)	
Urostomy ischemia	3 (5)	0 (0)	3 (8)	
Pulmonary embolism	1 (2)	0 (0)	1 (2)	
Wound hematoma	6 (10)	4 (17)	2 (5)	
12-mo UD-related sequelae, n (%)				
Uretero-ileal stricture	24 (6.5)	0 (0)	24 (13.7)	<0.001[a]
Parastomal hernia	8 (2.2)	0 (0)	8 (4.6)	
Peristomal hernia	3 (0.8)	0 (0)	3 (1.7)	
Stoma stenosis	5 (1.3)	0 (0)	5 (2.8)	
Calcolosis	4 (1)	0 (0)	4 (2.3)	

CD = Clavien-Dindo classification; EBL = estimated blood loss; IQR = interquartile ranges; RC = Radical Cystectomy; UD = Urinary diversion.
[a] Statistically significant.

$P = 0.005$), positive surgical margins (HR 2.30, $P = 0.005$), pN+ (HR 2.36, $P = 0.003$), pT≥3 (HR 1.32, $P = 0.02$), and current smoking status (HR 2.1, $P = 0.02$) were significant predictors of overall mortality.

3.5. RC-Pentafecta achievement

RC-Pentafecta achievement rates according to UD are depicted in Table 4. Patients receiving ONB had higher rate of overall RC- Pentafecta achievement (69.5% vs. 47.2%, $P = 0.004$) and absence of positive STM (98.8% vs. 92.2%, $P = 0.03$) when compared with patients receiving IC. At multivariable logistic regression model (Table 5), surgical experience (OR 1.2, $P < 0.001$), age at surgery (OR 0.93, $P = 0.04$), previous prostate surgery (OR 0.7, $P = 0.02$), UD type (1.9, $P = 0.04$), and pT stage ≥3 (OR 0.8, $P = 0.03$) were independent predictors of RC-Pentafecta achievement. The LOWESS function depicted a linear relationship between surgical experience and RC-Pentafecta achievement without reaching a plateau (Fig. 4).

4. Discussion

Several composite outcomes models, mainly trifecta and pentafecta, have been proposed over the last two decades to standardize and provide guidelines to define urological surgical quality [19,20]. Despite its complexity and high perioperative morbidity and mortality, validated surgical quality standards for RARC are still lacking. A previous RC-Pentafecta model, based on opinions of a panel of experts, was proposed by Aziz et al. to define optimal

Table 3
Oncological outcomes of 366 patients treated with robot-assisted RC.

Variable	Overall (n = 366)	RC-Pentafecta (n = 191)	No RC-Pentafecta (n = 175)	*P* value
Positive margins, n (%)				
Urothelial	5 (1.4)	3 (1.5)	2 (1.1)	<0.001[a]
Soft tissue	23 (6)	0 (0)	23 (13)	
N. Positive lymph nodes				
Median (IQR)	1 (1–1)	1 (1–1)	1 (1–1)	0.9
pT≥3, n (%)	131 (35.8)	64 (33)	67 (40)	0.04[a]
pT, n (%)				
pT0	40 (11)	20 (10.5)	20 (11.4)	0.05
pTIS	32 (8.7)	21 (11)	11 (6.3)	
pTa	12 (3.3)	7 (3.7)	5 (2.9)	
pT1	82 (22.4)	42 (22)	40 (22.9)	
pT2a	35 (9.6)	18 (9.4)	17 (9.7)	
pT2b	34 (9.3)	19 (10)	15 (8.6)	
pT3a	60 (16.4)	30 (15.7)	30 (17)	
pT3b	40 (11)	25 (13.1)	15 (8.6)	
pT4a	31 (8.3)	9 (4.6)	22 (12.6)	
pN, n (%)				
pN0	316 (86)	167 (88)	149 (86)	0.6
pN1	28 (7.6)	12 (6)	16 (9)	
pN2	22 (6.4)	12 (6)	10 (5)	
Recurrence ≤12 mo, n (%)	29 (8)	0 (0)	29 (16)	<0.001[a]
Site recurrence ≤12 mo, n (%)				
Local	5 (1.3)	0 (0)	5 (2.8)	<0.001[a]
Upper tract	2 (0.5)	0 (0)	2 (0.6)	
Distant	22 (6.2)	0 (0)	22 (12.6)	
Adjuvant chemotherapy, n (%)	29 (7.9)	15 (7.8)	14 (8)	0.8
Salvage chemotherapy, n (%)	52 (14)	22 (12)	30 (17)	0.7
Follow-up (months)				
Median (IQR)	29 (14–55)	30 (15–61)	28 (14–48)	0.7
Overall mortality, n (%)	134 (36)	50 (26)	84 (48)	<0.001[a]
Cancer specific mortality, n (%)	77 (21)	25 (13)	52 (30)	<0.001[a]

CD = Clavien-Dindo classification; EBL = estimated blood loss; IQR = interquartile ranges; RC = Radical Cystectomy; UD = Urinary diversion.
[a] Statistically significant.

outcomes after RC for muscle-invasive bladder cancer [20]. Of note, EAU guidelines suggest, with a high level of evidence, that RC should also be proposed to patients with high-risk or BCG unresponsive non-muscle invasive bladder cancer [21]. Cacciamani proposed a modification of the RC-Pentafecta, applicable both to muscle and non-muscle invasive bladder cancers, to provide a more comprehensive tool to standardize the surgical quality of RC [5]. We aimed to assess Cacciamani's RC-Pentafecta, considering the parameters as suggested by the authors, evaluating the rates of RC-Pentafecta achievement. Moreover, we assessed its impact on oncological outcomes and evaluated the role of surgical experience on RC-Pentafecta achievement, using a large single center intracorporeal RARC series with a mini-

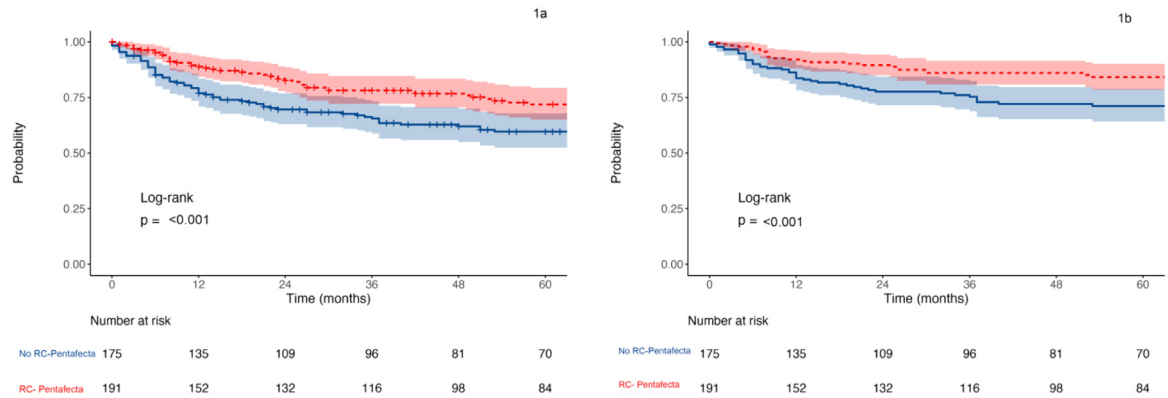

Fig. 1. Kaplan-Meier curves investigating overall survival (A) and cancer-specific mortality free-survival (B) of 366 patients who underwent RARC according to RC-Pentafecta achievement. RARC = robot-assisted radical cystectomy; RC = radical cystectomy.

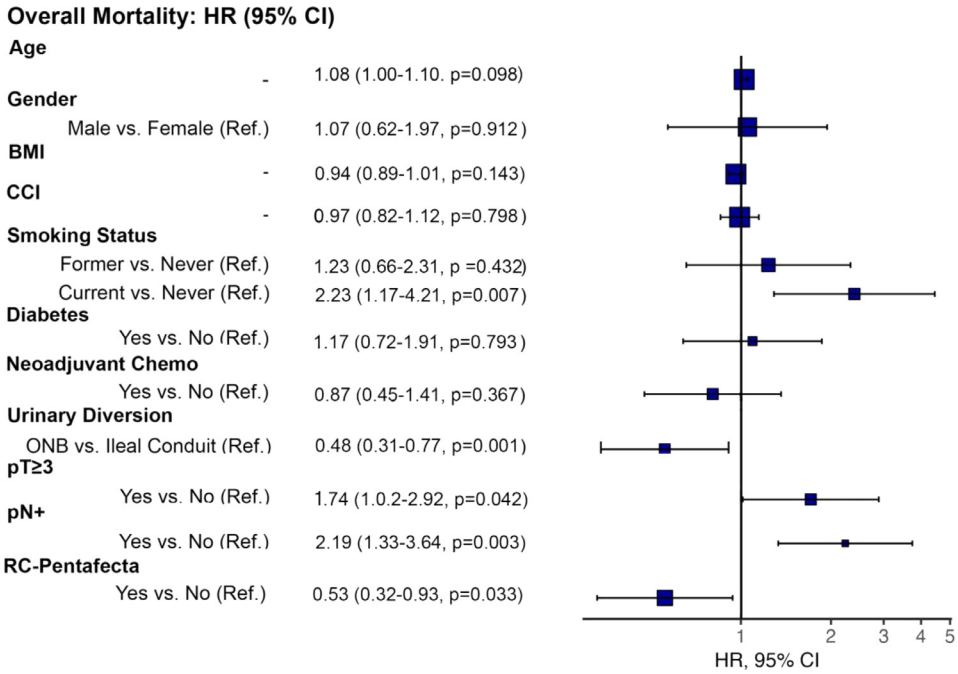

Fig. 2. Forest plot illustrating the results of multivariable Cox's proportional hazard regression model to predict overall mortality of 366 patients who underwent RARC. RARC = robot-assisted radical cystectomy.

mum of 1-year follow-up. Our analyses showed several noteworthy observations.

First, in our series RC-Pentafecta was achieved in 191 (52.2%) patients, a rate similar to that observed in the original study (53.3%) [5]. Absence of positive STM, absence of 90-day major complications, absence of ≤12-month recurrence, absence of ≤12-month UD-sequelae and ≥16 lymph nodes at the final pathological examination were recorded in 93.7%, 85.2%, 92.1%, 88%, and 75.7% of patients, respectively. The item most frequently preventing the achievement of RC-Pentafecta was the number of lymph nodes yielded at final pathology (44%). Of note, patients not achieving RC-Pentafecta had a median of 15 lymph nodes retrieved and a number of LNY between 10 and 15 is already considered suggestive of surgical quality of RC both by the Bladder Cancer Collaborative group [22] and by several retrospective studies [23,24]. We found age, previous prostate surgery, pT stage, and UD type to be significant predictors of RC-Pentafecta achievement at the multivariable logistic regression. Age could impact the RC-Pentafecta rates affecting complications rate, as suggested by Cacciamani in the original paper [5]. pT stage ≥3, conversely, may affect RC-Pentafecta achievement increasing the risk of ≤12-month recurrence [25]. Finally, as recently reported by Rosiello et al., patients with a history of previous prostatic surgery undergoing RARC may experience higher rates of perioperative complications [9], reducing the rates of RC-Pentafecta for male patients with a history of urological surgeries for prostate pathologies. In the present series, ONB was associated with higher rates of RC-Pentafecta. Although lower rates of RC-Pentafecta in patients receiving ONB were reported both in the original paper [5] and in manuscript by Oh [6], our data are supported by other series reporting lower rates of high-grade complications [26], as well as lower rates of recurrence [27] in patients receiving ONB when compared with patients with IC. Of note, patients receiving ONB were significantly younger (65 vs. 72 years, $P < 0.001$) and harbored less comorbidities (median CCI 3 vs. 4, $P < 0.001$), when compared with patients receiving other UD.

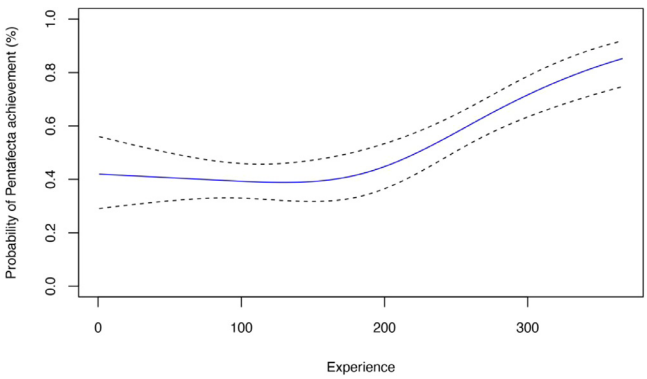

Fig. 3. Calibration plot illustrating calibration and discrimination of a regression model to predict overall mortality of 366 patients who underwent RARC. RARC = robot-assisted radical cystectomy.

Second, RC-Pentafecta achievement's association with better survival outcomes, when compared with patients failing to fulfill the requirements, was confirmed when applied to an independent external cohort of RARC. Five-year OS and 5-year CSS were significantly higher in patients who

Table 4
RC-Pentafecta achievement rate stratified for UD of 366 patients who underwent RARC.

Variable	Overall (n = 366)	Ileal conduit (n = 284)	Neobladder (n = 82)	*P* value
RC-Pentafecta, n (%)	191 (52.2)	134 (47.2)	57 (69.5)	0.004[a]
≥16 lymph node yielded, n (%)	277 (75.7)	211 (74.3)	66 (80.5)	0.2
Absence of positive STM, n (%)	343 (93.7)	262 (92.2)	81 (98.8)	0.03[a]
Absence of 90-d major complications, n (%)	312 (85.2)	237 (83.4)	75 (91.5)	0.07
Absence of ≤12-mo recurrence, n (%)	337 (92.1)	259 (91.2)	78 (95.1)	0.2
Absence of 12-mo UD sequelae, n (%)	322 (88)	249 (87.7)	73 (88)	0.7
RC-Pentafecta failing item, n (%)[b]				
≥16 lymph nodes yielded	54 (44)	45 (42)	9 (56)	0.05
Absence of positive STM	11 (9)	10 (9)	1 (6)	
Absence of 90-d major complications	26 (21)	23 (21)	3 (19)	
Absence of ≤12-mo recurrence	14 (11)	14 (13)	0 (0)	
Absence of ≤12-mo UD sequelae	18 (15)	15 (15)	3 (19)	

RARC = Robot-assisted Radical Cystectomy; STM = soft tissue margins; UD = urinary diversion.
[a] Statistically significant.
[b] In case of 4/5 items satisfied.

attained RC-Pentafecta when compared with patients who did not achieve it (71.8% vs. 59.6% and 84.1% vs. 71.1%, respectively). Noteworthy, the rates of both OS and CSS in the two groups showed to be higher than previously reported. Brassetti et al., in a study investigating oncological outcomes after RARC with ICUD using a multi-institutional series, reported 5-year OS and CSS of 54% and 61%, respectively [28]. In a comprehensive review investigating the current role of RARC, Fujimura reported 5-year OS rates ranging from 42% to 48% and 5-year CSS rates between 62% and 74% [29]. Moreover, at multivariable Cox's proportional hazard regression model, RC-Pentafecta achievement showed a protective effect (HR 0.57, $P = 0.03$) on overall mortality. This data was confirmed at sensitivity analysis including only patients undergoing RARC with ileal conduit. Finally, each item of RC-Pentafecta showed a significant correlation with OM and CSS. These findings are of utmost importance since they support the hypothesis that surgical experience may have an outstanding role in determining patients' long-term oncological outcomes. Moreover, they emphasize the role of Cacciamani's RC-Pentafecta as a valid tool to assess RC surgical quality and to define excellence's standard for RARC.

Table 5
Multivariable logistic regression predictive model of RC-Pentafecta achievement.

RC-Pentafecta achievement		
Variable	OR (95% CI)	*P* value
Surgical experience (continuous)	1.08 (1.01–1.1)	<0.001[a]
Age (continuous)	0.93 (0.1–0.98)	0.04[a]
Gender		
Male vs. Female	1.01 (0.5–2)	0.5
CCI (continuous)	0.96 (0.8–1.4)	0.6
BMI (continuous)	1 (1–1)	0.9
DM		
No vs. Yes	0.65 (0.3–1.3)	0.2
Smoking status		
Never vs. Current	0.9 (0.5–1.6)	0.73
Never vs. Former	0.9 (0.4–1.9)	0.79
Previous prostate surgery		
No vs. Yes	0.7 (0.4–0.97)	0.02[a]
NACH		
No vs. Yes	0.8 (0.4–1.5)	0.5
Urinary diversion		
Ileal Conduit vs. Neobladder	1.9 (1.2–3.8)	0.04[a]
pT stage		
pT≤2 vs. pT≥3	0.8 (0.4–0.99)	0.03[a]
pN stage		
pN+ vs. pN0	1.2 (0.8–1.3)	0.06

BMI = Body-mass index; CCI = Charlson Comorbidity Index; CI = confidence intervals; DM = Diabetes Mellitus; NACH = Neoajuvant chemotherapy; OR = odds ration; RC = Radical Cystectomy.
[a] Statistically significant.

Finally, our analysis showed a protective effect of surgical experience on RC-Pentafecta achievement (OR 1.08, $P < 0.001$, Table 4). We recorded a two-phase pattern regarding RC-Pentafecta achievement rates through surgical experience progression, characterized by an initial reduction of RC-Pentafecta achievement, followed by a rapid increment of achievement rates after 180 cases. Remarkably, the rates of RC-Pentafecta increased from 40% to 88% between cases 180 and 350 (Fig. 3). Our findings are supported by a recent study investigating the effects of surgical experience on perioperative and oncological outcomes in patients treated with RARC and ICUD [4]. The authors suggested a non-linear correlation between surgical experience and rates of major complications. Of note, we failed to observe a late plateau phase, suggesting that improvements may still be achieved, even for surgeons with extensive experience. These findings support the role of RC-Pentafecta as a tool to standardize surgical quality benchmarks and to provide guidelines to define "referral" centers for RARC.

The current study provides some remarkable information. First, we applied Cacciamani's RC-Pentafecta using a large series of RARC from a high-volume referral center. Second, we provided useful insight on the role of RARC's learning curve in achieving standardized quality outcomes.

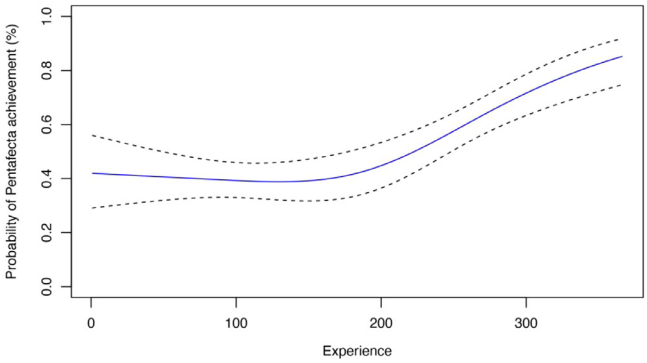

Fig. 4. Surgical learning curve for robot-assisted radical cystectomy: effect on the increasing surgical experience on RC-Pentafecta achievement. RC = radical cystectomy.

Third, the reliability of our data collection is high since all the quality criteria for accurate and comprehensive reporting of surgical outcomes recommended by EAU Guidelines on reporting and grading of complications were fulfilled (14/14 criteria satisfied). This is crucial to increase the rate of complications detected as recently demonstrated [30]. Despite its strengths, our study is not devoid of limitations. First, the study relied on a retrospective series, with all its inherent limitations. Second, we were unable to adjust for modification of surgical equipment over time. Third, in our center, elective cystectomies are performed only via robot-assisted surgery. As consequence, no comparison with the open approach was possible. Fourth, we reported data from highly experienced surgeons with a high annual caseload and extensive robotic experience. Therefore, these outcomes may not be generalizable to other centers.

5. Conclusions

RC-Pentafecta, proposed by Cacciamani et al., is a valuable tool to assess both the surgical quality of RARC and the experience of the center where the surgery is performed and may be used to identify "referral" center for treatment of high-risk bladder cancer.

Author disclosure statement

No competing financial interests exist.

Declaration of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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None

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urolonc.2022.01.001.

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