

**The Impact of the Implementation of the EAU Guidelines Panel
Recommendations on Reporting and Grading Complications on Perioperative
Outcomes after Robot-assisted Radical Prostatectomy**

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2 **Abstract**

3 The rate of postoperative complications might vary according to the method used to
4 collect perioperative data. We aimed at assessing the impact of the prospective
5 implementation of the EAU guidelines on reporting and grading of complications in
6 prostate cancer (PCa) patients undergoing robot-assisted radical prostatectomy
7 (RARP). From September 2016, an integrated method for reporting surgical
8 morbidity based on the EAU guidelines was implemented at a single, tertiary center.
9 Perioperative data were prospectively and systematically collected during a patient
10 interview at 30-day after surgery as recommended by the EAU Guidelines Panel
11 Recommendations on Reporting and Grading Complications. The rate and grading
12 of complications of 167 patients who underwent RARP ± pelvic lymph node
13 dissection (PLND) after the implementation of the prospective collection system
14 (Group 1) were compared with 316 patients treated between January 2015 and
15 August 2016 (Group 2) when a system based on patient chart review was used. No
16 differences were observed in disease characteristics and PLND between the two
17 groups (all $P \geq 0.1$). Postoperative complications were graded according to the
18 Clavien-Dindo system. Overall, the complication rate was higher when the
19 prospective collection system based on the EAU guidelines was used (29%) as
20 compared to retrospective chart review (10%; $P < 0.001$). In particular, a substantially
21 higher rate of grade 1 (8.4 vs. 4.7%) and 2 (14 vs. 2.8%) complications was detected
22 in Group 1 vs. Group 2 ($P < 0.001$). Although the rate of complications occurred
23 during hospitalization did not differ (13 vs. 10%; $P = 0.3$), 31 (19%) complications after
24 discharge were detected in Group 1. This resulted into a readmission rate of 16%.
25 Conversely, no complications after discharge and readmissions were recorded for
26 Group 2. The implementation of the EAU guidelines on reporting perioperative

27 outcomes roughly doubled the complication rate after RARP and allowed for the
28 detection of complications after discharge in more than 15% of patients that would
29 have been otherwise missed, where patients assessed with the EAU implemented
30 protocol had a 3-fold higher likelihood of reporting complications.

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32 **Patient summary**

33 The implementation of the EAU guidelines on reporting and grading of complications
34 after urologic procedures in prostate cancer patients roughly doubled the
35 complication rate after robot-assisted radical prostatectomy compared to
36 retrospective patient chart review. Moreover, it allowed for the detection of
37 complications after discharge in more than 15% of patients that would have been
38 otherwise missed.

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40 **Take home message**

41 The implementation of the EAU guidelines on reporting and grading of complications
42 after urologic procedures roughly doubled the complication rate after RARP in
43 prostate cancer patients and allowed for the detection of complications after
44 discharge in more than 15% of patients that would have been otherwise missed.

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46 Perioperative outcomes (i.e., morbidity and mortality) after surgical procedures
47 represent well-established proxies of quality of care [1]. When considering localized
48 prostate cancer (PCa), the rate of postoperative complications after robot-assisted
49 radical prostatectomy (RARP) ranges between 3 and 40% and varies according to
50 patient characteristics, technique and surgical experience [2, 3]. Nonetheless,
51 heterogeneity in the definition of complications and assessment tools might in part
52 explain such a huge variability in reported outcomes, where the adoption of
53 standardized definitions and data collection systems would allow for a better
54 characterization of surgical results, comparison of surgeons or techniques and
55 preoperative counseling [3-6]. The EAU guideline panel recently released ad hoc
56 recommendations on reporting and grading of complications after urologic
57 procedures [7]. We aimed to assess the impact of the prospective implementation of
58 these guidelines on the rate of postoperative complication in a large contemporary
59 cohort of PCa patients undergoing RARP at a tertiary center.

60 After IRB approval, 500 patients with clinically localized PCa who underwent RARP ±
61 extended pelvic lymph node dissection (ePLND) between January 2015 and
62 September 2017 at a single center were identified. All surgical procedures were
63 performed by three surgeons with at least 100 cases at the beginning of data
64 collection using the same technique to limit potential biases related to the learning-
65 curve phenomenon [8, 9]. Starting from September 2016 a prospective collection
66 system for perioperative outcomes based on patient interview done by medical
67 doctors at 30-day after surgery was implemented. The quality criteria for accurate
68 and comprehensive reporting of surgical outcomes recommended by the EAU
69 guidelines on reporting and grading of complications were fulfilled (Table 1) [5, 7].
70 Overall, 17 (3.4%) patients treated after the implementation of the prospective

71 collecting system did not complete the interview at 30-day and were excluded from
72 our analyses. This resulted in a final population of 483 patients. The rate and grading
73 of complications of 167 consecutive patients who underwent RARP after the
74 implementation of the prospective collection system (Group 1) were compared with
75 316 patients treated between January 2015 and August 2016 when a collection
76 system based on patient chart review done by two dedicated data managers was
77 used (Group 2). In the latter group, only events occurred during the hospital stay at
78 the treating institution were collected. Postoperative complications were graded
79 according to the Clavien-Dindo system [10]. The Mann-Whitney test was used to
80 assess differences in distributions of continuous variables between the two groups.
81 The chi-square test compared differences in proportions between the two groups.
82 Multivariable logistic regression analyses assessed the impact of the implementation
83 of the EAU guidelines on the probability of detecting postoperative complications
84 after adjusting for potential confounders.
85 Median age at surgery was 64.5 years. Overall, 82 (17%), 283 (59%) and 118 (24%)
86 patients had low-, intermediate-, and high-risk disease, respectively. Of all men, 356
87 (73%) received an ePLND. No differences were observed in baseline disease
88 characteristics, pathologic features and the use of ePLND between the two groups
89 (all $P \geq 0.1$; Supplementary Table). No significant differences in baseline variables
90 were detected between patients included vs. those excluded from the final cohort
91 ($P \geq 0.1$). Median blood loss and length of stay (LoS) were 150 ml and 3 days and did
92 not differ between the two groups (Table 2). Median operative time was 175 vs. 185
93 min for patients in group 1 vs. 2, respectively ($P=0.02$). Overall, 81 (17%) patients
94 experienced postoperative complications. The overall complication rate was
95 significantly higher when a prospective collection system based on the EAU

96 guidelines was used (group 1; 29%) as compared to retrospective chart review
97 (group 2; 10%; $P < 0.001$). A significantly higher rate of grade 1 and 2 complications
98 was detected for patients included in Group 1 vs. Group 2 (8.4 vs. 4.7% and 14 vs.
99 2.8% for grade 1 and 2 complications, respectively; $P < 0.001$). Similarly, the
100 implementation of a prospective collection system resulted into the detection of a
101 higher rate of procedure specific complications such as anastomotic leak (7.8 vs.
102 1.9%), anaemia (3.6 vs. 0.6%) and lymphocele (3.0 vs. 0.3%; all $P \leq 0.02$) as
103 compared to retrospective chart review. Although the rate of complications occurred
104 during hospitalization did not differ between the two groups (13 vs. 10%; $P = 0.3$), the
105 implementation of a prospective collection system resulted in the identification of
106 complications after discharge in 31 (19%) patients that would have been otherwise
107 missed. This translated into a readmission rate of 16%. These results were
108 confirmed even after assuming that all patients with missing data did or did not
109 experience complications (all $P < 0.001$). Finally, the association between the
110 implementation of the EAU guidelines and the complication rate was confirmed also
111 in multivariable analyses after adjusting for age, risk groups and Charlson
112 comorbidity index (Odds ratio: 3.40; 95% Confidence Interval: 2.07-5.5;
113 Supplementary Table 2).

114 The rate of complications after RARP is highly heterogeneous, with several studies
115 reported excellent perioperative outcomes [2]. However, the majority of these series
116 did not apply a rigorous standardized approach to collect perioperative data.
117 Conversely, the use of standardized methods for collecting and reporting
118 postoperative outcomes typically results into higher rates of postoperative
119 complications [3, 6, 7, 11]. Under this light, our study represents the first attempt to
120 validate the EAU guidelines on reporting and grading of complications in the clinical

121 scenario [7]. In particular, we were able to assess the impact of the implementation
122 of the EAU guidelines in a series of consecutive patients treated at a single center by
123 high-volume surgeons under similar circumstances. The implementation of the EAU
124 recommendations and the assessment of perioperative outcomes using a patient
125 interview at 30-day substantially increased the complications detected as compared
126 to patient chart review. Although no differences were observed when considering
127 events occurred during hospitalization, a prospective assessment allowed for the
128 detection of complications after discharge in more than 18% patients that would have
129 been otherwise missed. The main impact of the implementation of a prospective
130 collection system was on grade 1 and 2 complications and is likely related to the
131 more rigorous reporting of the data [6]. It should also be noted that the prospective
132 collection system led to the detection of a higher number of procedure-specific
133 complications such as lymphoceles, anemia and anastomotic leaks that typically
134 occur after patient discharge and may have a significant clinical impact.

135 These observations have important implications for clinicians evaluating
136 perioperative outcomes of RARP. First, the evaluation of morbidity as a proxy of
137 surgical quality is only justified when patients are carefully followed-up in the
138 perioperative period and for surgeons who are aware of their own results. Second, a
139 standardized collection system fulfilling predefined quality criteria should be used
140 when comparing perioperative outcomes between different surgical techniques.
141 Third, the adoption of a rigorous method to collect surgical outcomes would result in
142 detailed patterns of complications thus improving patient management in the post-
143 operative period. Finally, only the use of a rigorous method for the detection of
144 perioperative complications would allow for a comprehensive preoperative patient
145 counseling regarding the side effects of a surgical procedure.

146 Concluding, the implementation of the EAU guidelines on reporting perioperative
147 outcomes roughly doubled the complication rate after RARP and allowed for the
148 detection of complications after discharge in more than 15% of patients that would
149 have been otherwise missed, where patients assessed with the EAU implemented
150 protocol had a 3-fold higher likelihood of reporting complications after accounting for
151 confounders. Clinicians should rely on studies using a rigorous standardized method
152 to collect perioperative data and fulfilling predefined quality criteria when evaluating
153 the surgical outcomes of RARP.

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155 **Conflicts of interest:** The authors have nothing to disclose.

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193 **Supplementary Table 1.** Clinical and pathologic characteristics of patients included
 194 in the study.
 195

	Overall (n=483)	Group 1 (n=167; 35%)	Group 2 (n=316; 65%)	p-value
Age at surgery (years) Median (IQR)	65 (59-69)	65 (59-69)	64 (59-69)	0.6
CCI (%) 0 1 ≥2	407 (84) 61 (12) 15 (3.1)	144 (86) 18 (11) 5 (3.0)	263 (83) 43 (14) 10 (3.1)	0.7
Preoperative PSA (ng/ml) Median (IQR)	6.6 (4.7-9.8)	7.0 (4.8-9.9)	6.5 (4.7-9.5)	0.9
Clinical stage (%) T1 T2 T3	272 (56) 161 (33) 50 (10)	102 (61) 45 (27) 20 (13)	170 (54) 116 (37) 30 (9.5)	0.1
Biopsy ISUP grade group (%) 1 2 3 4 5	118 (24) 189 (39) 98 (20) 43 (8.9) 35 (7.2)	36 (22) 66 (39) 33 (20) 20 (12) 12 (7.2)	82 (26) 123 (39) 65 (21) 23 (7.3) 23 (7.3)	0.4
Risk group (%) Low Intermediate High	82 (17) 283 (59) 118 (24)	24 (14) 96 (58) 47 (28)	58 (18) 187 (59) 71 (23)	0.3
Pathologic stage (%) pT2 pT3a pT3b-4	221 (46) 190 (39) 72 (15)	75 (45) 68 (41) 24 (14)	146 (46) 122 (39) 48 (15)	0.8
Positive surgical margins (%)	113 (24)	35 (22)	78 (25)	0.2
Pathologic grade group (%) 1 2 3 4 5	35 (7.2) 189 (39) 149 (31) 32 (6.6) 78 (16)	9 (5.4) 72 (43) 53 (32) 11 (6.6) 22 (13)	26 (8.2) 117 (37) 96 (30) 21 (6.6) 56 (18)	0.4
Pathologic nodal stage (%) pNx pN0 pN1	127 (27) 284 (58) 66 (15)	38 (24) 99 (61) 25 (15)	89 (28) 185 (59) 41 (13)	0.4
Surgeon (%) 1 2 3	308 (63.8) 97 (20.1) 78 (16.1)	114 (68.3) 27 (16.2) 26 (15.6)	194 (61.4) 70 (22.2) 52 (16.5)	0.2
CCI: Charlson comorbidity index				

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198 **Supplementary Table 2.** Multivariable analyses assessing the impact of the
 199 implementation of a prospective collection system based on the EAU guidelines on
 200 reporting and grading of complications in prostate cancer (PCa) patients undergoing
 201 robot-assisted radical prostatectomy (RARP).

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	Odds Ratio	95% Confidence Interval	p- value
Implementation of the EAU guidelines on reporting and grading of complications	3.40	2.07-5.51	<0.001
Age at surgery	0.99	0.95-1.03	0.5
Charlson Comorbidity Index			
0	1 (Ref.)		
1	1.41	0.68-2.89	0.2
≥2	0.81	0.35-3.94	0.8
Risk group			
Low-risk	1 (Ref.)		
Intermediate-risk	1.54	0.70-3.36	0.3
High-risk	2.14	0.91-5.01	0.1

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205 **Table 1.** Quality criteria for accurate and comprehensive reporting of surgical
 206 outcome and their implementation to collect postoperative complications in prostate
 207 cancer (PCa) patients treated with robot-assisted radical prostatectomy (RARP) at a
 208 single tertiary referral center.

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	Criteria	Implementation
1	Define the method of accruing data	Prospective data collection based on a patient interview conducted by telephone
2	Define who collected the data	Data were collected by medical doctors who were not involved in the treatment
3	Indicate the duration of follow-up	30 days
4	Include outpatient information	Outpatient information were collected
5	Include mortality data and causes of death	Mortality data were collected
6	Include definitions of complications	Surgical complications were defined as any deviation from the ideal postoperative course that is not inherent in the procedure and does not comprise a failure to cure
7	Define procedure-specific complications	Procedure-specific complications were defined and collected
8	Report intraoperative and postoperative complications separately	Intraoperative and postoperative complications were considered separately
9	Use a severity grading system for postoperative complications	The Clavien-Dindo system was used
10	Postoperative complications should be presented in a table either by grade or by complication type	Postoperative complications were graded according to the Clavien-Dindo system and presented in a table
11	Include risk factors	The Charlson comorbidity index was prospectively collected for all patients
12	Include readmissions and cause	Data on readmissions were specifically collected
13	Include re-operations, types and causes	Data on reoperations were collected
14	Include the percentage of patients lost to follow-up	17 (3.4%) patients had incomplete information on 30-day complications and were excluded from the current analysis

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211

212 **Table 2.** Perioperative outcomes of prostate cancer (PCa) patients treated with radical
 213 prostatectomy (RP) ± extended pelvic lymph node dissection (ePLND). A prospective
 214 collection system based on the EAU guidelines on reporting and grading of complications
 215 was implemented for patients included in Group 1. A collection system based on patient
 216 chart review was used for patients included in Group 2.

217

	Overall (n=483)	Group 1 (n=167; 35%)	Group 2 (n=316; 65%)	p- value
Operative time (min) Median (IQR)	180 (158-210)	175 (151-206)	185 (159-213)	0.02
Blood loss (ml) Median (IQR)	150 (100-250)	150 (100-250)	150 (100-250)	0.9
30-day complications (%)				
Overall	81 (17)	48 (29)	33 (10)	<0.001
During hospitalization	54 (11)	21 (13)	33 (10)	0.3
After discharge	31 (6.4)	31 (19)	0 (0)	<0.001
Clavien-Dindo classification (%)				
1	29 (6.0)	14 (8.4)	15 (4.7)	<0.001
2	32 (6.6)	23 (14)	9 (2.8)	
3	17 (3.5)	8 (4.8)	9 (2.8)	
4	1 (0.2)	1 (0.6)	0 (0)	
5	0 (0)	0 (0)	0 (0)	
Procedure-specific complications (%)				
Anastomotic leak	19 (3.9)	13 (7.8)	6 (1.9)	0.01
Anemia	8 (1.7)	6 (3.6)	2 (0.6)	0.02
Lymphocele	6 (1.2)	5 (3.0)	1 (0.3)	0.01
Rectal injury	0 (0)	0 (0)	0 (0)	NA
Postoperative transfusion (%)	5 (1.1)	0 (0)	5 (1.7)	0.1
Reoperation (%)	8 (1.7)	5 (3.0)	3 (0.9)	0.1
Length of stay (days) Median (IQR)	3 (2-3)	3 (2-3)	3 (2-3)	0.2
Readmission (%)	27 (5.6)	27 (16)	0 (0)	<0.001

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220 **Take home message**

221 The implementation of the EAU guidelines on reporting and grading of complications
222 after urologic procedures roughly doubled the complication rate after RARP in PCa
223 patients and allowed for the detection of complications after discharge in more than
224 15% of patients that would have been otherwise missed.

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