

Robot-assisted versus other types of radical prostatectomy: Population-based safety and cost comparison in Japan, 2012–2013

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In 2012, Japanese national insurance started covering robot-assisted surgery. We carried out a population-based comparison between robot-assisted and three other types of radical prostatectomy to evaluate the safety of robot-assisted prostatectomy during its initial year. We abstracted data for 7202 open, 2483 laparoscopic, 1181 minimal incision endoscopic, and 2126 robot-assisted radical prostatectomies for oncological stage T3 or less from the Diagnosis Procedure Combination database (April 2012–March 2013). Complication rate, transfusion rate, anesthesia time, postoperative length of stay, and cost were evaluated by pairwise one-to-one propensity-score matching and multivariable analyses with covariants of age, comorbidity, oncological stage, hospital volume, and hospital academic status. The proportion of robot-assisted radical prostatectomies dramatically increased from 8.6% to 24.1% during the first year. Compared with open, laparoscopic, and minimal incision endoscopic surgery, robot-assisted surgery was generally associated with a significantly lower complication rate (odds ratios, 0.25, 0.20, 0.33, respectively), autologous transfusion rate (0.04, 0.31, 0.10), homologous transfusion rate (0.16, 0.48, 0.14), lower cost excluding operation (differences, –5.1%, –1.8% [not significant], –10.8%) and shorter postoperative length of stay (–9.1%, +0.9% [not significant], –18.5%, respectively). However, robot-assisted surgery also resulted in a +42.6% increase in anesthesia time and +52.4% increase in total cost compared with open surgery (all $P < 0.05$). Introduction of robotic surgery led to a dynamic change in prostate cancer surgery. Even in its initial year, robot-assisted radical prostatectomy was carried out with several favorable safety aspects compared to the conventional surgeries despite its having the longest anesthesia time and the highest cost.

Prostate cancer is a global public health issue, and radical prostatectomy has been widely recognized as a standard treatment for patients with localized disease.⁽¹⁾ The open approach was traditionally carried out. However, after the development of laparoscopic technology and the use of surgical robotic devices, minimally invasive approaches have steadily become more popular. The use of RARP, especially, has spread rapidly in the USA and Europe. Several RCTs, systematic reviews, and meta-analyses have described the superiority of RARP over LRP and ORP in terms of blood loss, complications, incontinence, and loss of sexual function.^(2–8)

Compared to North America and European countries, the introduction of minimally invasive radical prostatectomy in Japan was rather different. National universal health care insurance officially began covering LRP in 2006 and MIE-RP (gasless single-port-access endoscopic surgery) in 2008. The restriction for RARP was not lifted until April 2012. Even though RARP was a latecomer to the surgical armamentarium in Japan, the number of robotic sur-

geries increased dramatically after its approval. Japan soon had the second largest number of surgical robots worldwide.⁽⁹⁾ This abrupt prevalence of RARP usage caused some concern about the skillfulness of surgeons with this new technology. Although it was generally thought that the learning curve for robot-assisted surgery was shorter than that for other minimally invasive operations, there was a high incidence of complications reported in the initial cases.⁽¹⁰⁾ Thus, an outcomes study involving a large number of institutions became necessary to verify the safety and feasibility of RARP compared with conventional prostatectomy approaches. The aim of the present study was to evaluate perioperative outcomes among four types of radical prostatectomy during the initial year of RARP application. For the study group, we relied on a Japanese population-based database.

Material and Methods

Data source for the study. The comparisons in the current study were carried out based on the DPC database, a Japanese

inpatient administrative claims database. In 2012, it had data of 6 852 195 hospitalizations from 1057 participating hospitals, representing approximately 50% of acute care hospitalizations throughout Japan.⁽¹¹⁾ This database holds clinical information on such areas as: (i) the main diagnoses, comorbidities at admission, and complications after admission; (ii) surgical procedures; (iii) discharge status; and (iv) use of medical resources. Diagnoses were coded according to the ICD-10. Because the data in the DPC database were thoroughly de-identified and the present study was designed as a secondary analysis of the administrative claims data, informed consent was not required. The institutional review board and ethics committee of The University of Tokyo (Tokyo, Japan) approved the study.

Data sampling and measured outcomes. Selected patients were those undergoing ORP, LRP, MIE-RP, or RARP (Japanese surgical codes K843, K843-2, K843-3, and K939-4, respectively) for the main diagnosis of malignant neoplasm of the prostate (ICD-10 code C61) from April 2012 to March 2013. Minimum incision endoscopic radical prostatectomy is a technique using a single, small incision that permits extraction of the specimen without gas insufflation, trocar ports, or injury to the peritoneum.⁽¹²⁾

Available baseline characteristics about the patient and hospital were age, comorbidities at admission, body mass index, smoking index (pack-year), oncological stage (according to the International Union Against Cancer),⁽¹³⁾ hospital academic status (academic or non-academic), and hospital volume (annual caseload of radical prostatectomy at each hospital). Comorbidities were converted to a score of the CCI according to Quan *et al.*⁽¹⁴⁾

The outcomes assessed were perioperative complications (see Table S1), blood transfusion, anesthesia time, postoperative length of stay, and costs including and excluding the operation. The costs were calculated at the currency rate of ¥100 = \$US1.

Statistical analysis. For univariable comparisons, the χ^2 -test and Mann–Whitney *U*-test were adopted, as appropriate. The threshold for significance was $P < 0.05$.

To improve the quality of comparisons, multiple imputation and propensity-score matching was carried out as follows. First, because there were some missing values for the body mass index, smoking index, and oncological stage, we per-

formed multiple imputation to replace each missing value with a set of substituted plausible values by creating five filling-in copies to reduce bias caused by incomplete data.^(15,16) In the process of missing imputation, predictive mean matching and polytomous regressions were used appropriately. After imputation, patients with T4, N+, or M+ were removed because of their small numbers. Second, in each imputed copy, one-to-one propensity-score matching was performed pairwise three times (i.e., RARP vs ORP, RARP vs LRP, and RARP vs MIE-RP).⁽¹⁷⁾ This matching methodology mimics randomized allocations to case and control groups, consequently reducing the bias that occurs because of the lack of randomization. A probability of allocation in the RARP group was estimated in each subject as a propensity score based on a logistic regression model incorporating potential confounders: age, CCI, body mass index, smoking index, oncological stage, hospital academic status, and hospital volume. The matching was executed using the nearest neighborhood approach with a caliper width equal to 0.2 of the standard deviation of the propensity score.⁽¹⁸⁾ Third, after matching, multivariable linear or logistic regression analyses were carried out for each outcome with covariates—type of radical prostatectomy, age, CCI, body mass index, smoking index, oncological stage, hospital academic status, hospital volume—in each imputed copy. In these multivariable models, generalized estimating equations were applied to adjust for hospital clustering effects.⁽¹⁹⁾ Finally, the results of the five imputed copies were combined into one model, from which the statistical inference was taken. The values of anesthesia time, postoperative length of stay, and costs were log-transformed in the linear regression models because of their skewed distributions. All statistical analyses were carried out using R version 3.0.2 software (R Foundation for Statistical Computing, Vienna, Austria) with RMS 4.0-0, Zelig 4.1-3, Mice 2.17, and MatchIt 2.4-21 packages.^(15,20–24)

To confirm the trend change for radical prostatectomy, a frequency distribution in the caseloads for four types of radical prostatectomy was determined, and the trend was analyzed using the Cochran–Armitage trend test.

Results

During the study period, 7202 ORP (55.4%), 2483 LRP (19.1%), 1181 MIE-RP (9.1%), and 2126 RARP cases (16.4%)

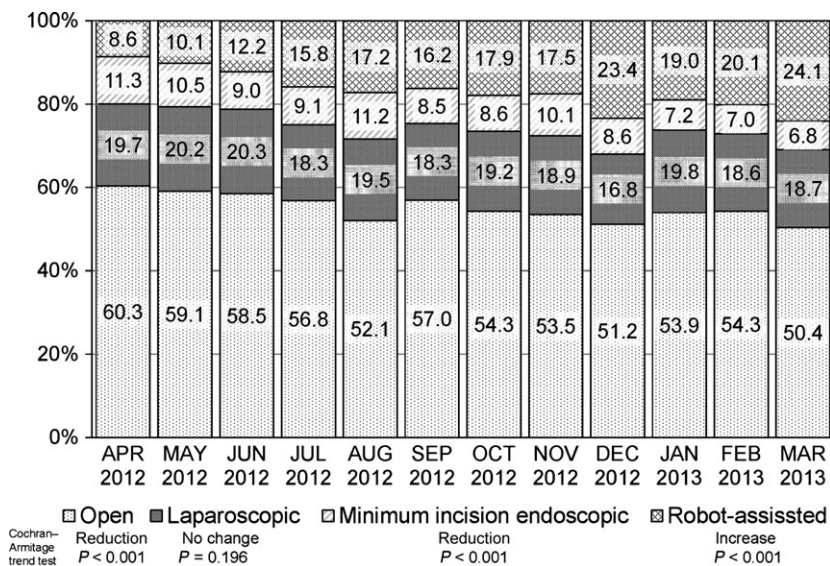


Fig. 1. Chronological trends for the four types of radical prostatectomy in Japan's Diagnosis Procedure Combination database between April 2012 and March 2013.

Table 1. Patient baseline characteristics among four types of radical prostatectomy registered in the Japanese Diagnosis Procedure Combination database between April 2012 and March 2013

Characteristic	Type of radical prostatectomy, <i>n</i> (%) or median (IQR)				<i>P</i> -value
	Open	Laparoscopic	MIE-RP	Robot-assisted	
Total	7202 (100.0)	2483 (100.0)	1181 (100.0)	2126 (100.0)	
No. of hospitals	552	90	68	45	
Age, years	68 (64–72)	68 (64–71)	67 (63–71)	67 (62–71)	<0.001
Charlson comorbidity index					
0	5405 (75.0)	1877 (75.6)	887 (75.1)	1908 (89.7)	<0.001
1	1167 (16.2)	409 (16.5)	196 (16.6)	166 (7.8)	
≥2	630 (8.7)	197 (7.9)	98 (8.3)	52 (2.4)	
Body mass index	23.7 (22.0–25.6)	23.8 (22.0–25.7)	23.7 (22.0–25.5)	23.7 (22.1–25.6)	0.497
Missing	48 (0.7)	15 (0.6)	39 (3.3)	13 (0.6)	
Smoking index, pack-year	0 (0–30)	5 (0–35)	8 (0–35)	0 (0–26)	<0.001
Missing	870 (12.1)	363 (14.6)	207 (17.5)	445 (20.9)	
Stage					
T1	1701 (23.6)	707 (28.5)	255 (21.6)	961 (45.2)	<0.001
T2	3941 (54.7)	1244 (50.1)	608 (51.5)	879 (41.3)	
T3	772 (10.7)	152 (6.1)	148 (12.5)	122 (5.7)	
T4, N+, or M+	161 (2.2)	32 (1.3)	25 (2.1)	14 (0.7)	
Missing	627 (8.7)	348 (14.0)	145 (12.3)	150 (7.1)	
Type of hospital					
Academic	1102 (15.3)	1267 (51.0)	335 (28.4)	1594 (75.0)	<0.001
Non-academic	6100 (84.7)	1216 (49.0)	846 (71.6)	532 (25.0)	
Hospital volume	25 (14–40)	61 (34–91)	34 (22–50)	96 (59–155)	<0.001
<i>Perioperative outcome</i>					
Autologous transfusion	5951 (82.6)	1038 (41.8)	835 (70.7)	260 (12.2)	<0.001
Homologous transfusion	523 (7.3)	56 (2.3)	68 (5.8)	15 (0.7)	<0.001
Overall complications	380 (5.3)	98 (3.9)	48 (4.1)	18 (0.8)	<0.001
Sepsis/DIC	15 (0.2)	4 (0.2)	1 (0.1)	2 (0.1)	0.600
Pulmonary embolism	14 (0.2)	2 (0.1)	1 (0.1)	1 (0.0)	0.288
Cardiac events	80 (1.1)	34 (1.4)	6 (0.5)	3 (0.1)	<0.001
Vascular complications	49 (0.7)	4 (0.2)	3 (0.3)	2 (0.1)	<0.001
Respiratory complications	35 (0.5)	16 (0.6)	3 (0.3)	4 (0.2)	0.085
Peritonitis or peritoneal abscess	16 (0.2)	7 (0.3)	2 (0.2)	0 (0.0)	0.139
Ileus	20 (0.3)	2 (0.1)	2 (0.2)	4 (0.2)	0.309
Genitourinary complications	63 (0.9)	26 (1.0)	9 (0.8)	1 (0.0)	<0.001
Disruption of operation wound	68 (0.9)	3 (0.1)	9 (0.8)	1 (0.0)	<0.001
Colorectal injury	34 (0.5)	7 (0.3)	6 (0.5)	0 (0.0)	0.010
Other intraoperative complications	23 (0.3)	4 (0.2)	9 (0.8)	0 (0.0)	<0.001
Others†	25 (0.3)	5 (0.2)	5 (0.4)	1 (0.0)	0.079
Anesthesia time, min‡	268 (223–323)	329 (270–386)	304 (252–356)	322 (279–382)	<0.001
Postoperative length of stay, days‡	14 (11–17)	11 (9–14)	13 (11–17)	11 (9–13)	<0.001
Total costs, \$US‡§	10 946 (10 098–12 035)	14 160 (13 409–15 121)	12 911 (12 063–14 147)	15 676 (14 984–16 495)	<0.001
Costs excluding operation, \$US‡§	4616 (3940–5526)	4208 (3527–4982)	4642 (3878–5855)	4434 (3758–5123)	<0.001

†The number of events was 10 or less. In-hospital mortality ($n = 9$, $P = 0.22$), pseudomembranous enterocolitis ($n = 5$, $P = 0.10$), stroke ($n = 9$, $P = 0.87$), pneumonia or flu ($n = 10$, $P = 0.56$), and acute renal failure ($n = 5$, $P = 0.40$). ‡Values were transformed into log-10 values for the modeling because of their skewed distributions. §\$US1 = ¥100. DIC, disseminated intravascular coagulopathy; IQR, interquartile range; MIE-RP, minimal incision endoscopic radical prostatectomy.

were abstracted from 552, 90, 68, and 45 institutes in the DPC database. The number of cases accounted for approximately 60% of all radical prostatectomies carried out in Japan.⁽²⁵⁾ Figure 1 shows the chronological trend for the four types of radical prostatectomy between April 2012 and March 2013. The proportion of RARP increased by approximately 2.8 times during the 12 months (from 8.6% to 24.1%; Cochran–Armitage

trend test, $P < 0.001$), whereas ORP and MIE-RP lost their share ($P < 0.001$). Table 1 presents the details of the patient baseline characteristics and the outcomes without background adjustment. In general, compared to the three conventional radical prostatectomies, RARP was carried out in patients with a slightly younger age, lower CCI, and earlier oncological stage at the institutions with high hospital volume and academic sta-

Table 2. Multivariate regression analyses for propensity-score-adjusted outcomes among robot-assisted radical prostatectomy (RARP) versus three other types of radical prostatectomy registered in the Japanese Diagnosis Procedure Combination database between April 2012 and March 2013

Parameter	RARP versus ORP		RARP versus LRP		RARP versus MIE-RP	
	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value
Average no. of pairs	989		1407		592	
No. of hospitals included	45 vs 163		45 vs 77		43 vs 57	
<i>Logistic regression model (odds ratio)</i>						
Overall complications	0.25 (0.15–0.41)	<0.001	0.20 (0.13–0.31)	<0.001	0.33 (0.18–0.64)	<0.001
Autologous transfusion	0.04 (0.03–0.05)	<0.001	0.31 (0.26–0.38)	<0.001	0.10 (0.07–0.14)	<0.001
Homologous transfusion	0.16 (0.08–0.32)	<0.001	0.48 (0.25–0.91)	0.025	0.14 (0.06–0.33)	<0.001
<i>Linear regression model (difference in percentage)</i>						
Anesthesia time, min†	+42.6% (39.0–46.2)	<0.001	+6.9% (5.0–8.8)	<0.001	+23.9% (20.4–27.4)	<0.001
Postoperative length of stay†	−9.1% (−12.0 to −6.2)	<0.001	+0.9% (−1.5 to 3.4)	0.459	−18.5% (−21.5 to −15.4)	<0.001
Total costs, \$US†‡	+52.4% (49.5–55.4)	<0.001	+13.2% (11.9–14.6)	<0.001	+22.8% (19.7–26.1)	<0.001
Costs excluding operation, \$US†‡	−5.1% (−7.3 to −2.9)	<0.001	−1.8% (−4.4 to 0.9)	0.195	−10.3% (−13.0 to −7.4)	<0.001

The effect of hospital clustering was regulated by generalized estimating equations. †Values were transformed into log-10 values for the modeling because of their skewed distributions. ‡\$US1 = ¥100. CI, confidence interval; LRP, laparoscopic radical prostatectomy; MIE-RP, minimal incision endoscopic radical prostatectomy.

tus. Regarding outcomes, low incidences of transfusion and complications drew our attention. After the process of missing imputation and the subsequent one-to-one propensity-score matching process, 989, 1407, and 592 pairs (on average) were generated between RARP versus ORP, RARP versus LRP, and RARP versus MIE-RP Table S2. Average C-statistics of the propensity score for each matching were 0.933, 0.757, and 0.898, respectively. After the matching, the background variations were closely balanced (data not shown).

Table 2 shows the results of the multivariable regression analyses for the outcomes. Compared with ORP, LRP, and MIE-RP, RARP was generally associated with a significantly lower complication rate (odds ratios 0.25, 0.20, 0.33, respectively), autologous transfusion rate (0.04, 0.31, 0.10, respectively), and homologous transfusion rate (0.16, 0.48, 0.14, respectively) as well as lower cost excluding operation (differences, −5.1%, −1.8% [not significant], −10.8%) and a shorter postoperative length of stay (−9.1%, +0.9% [not significant], −18.5%, respectively). However, RARP also showed a +42.6% increase in anesthesia time and a +52.4% increase in total cost compared with open surgery. The postoperative length of stay for the RARP group was comparable to that for the LRP group.

Discussion

This study is the first to compare perioperative outcomes between RARP and conventional radical prostatectomies in Japan at the national level. We knew that with 2012 being the first year of RARP approval by the Japanese national universal health care insurance the accumulation of experience with RARP would be limited. Despite that, by using a national database population for our analysis of perioperative outcomes, we showed that RARP was associated with substantially lower incidences of transfusion use and complications. We also found that the high total cost of RARP must be kept in mind.

Fewer than 20 hospitals in Japan had surgical robots at the end of 2011. It was reported, however, that the plan was to introduce more than 100 surgical robots by the end of 2013 throughout Japan.⁽⁹⁾ According to our data, RARP, which in April 2012 had the smallest share among the four types of rad-

ical prostatectomy that we studied, steadily increased its case-load and became the second most popular approach after the first 12 months of its availability. In the face of this dynamic change, it is essential to evaluate the safety and feasibility of RARP compared with other conventional surgeries. The present study provided a comprehensive answer that RARP successfully produced satisfactory performance at least in terms of perioperative outcomes during its initial year in Japan. The most distinctive feature was the difference in transfusion use between ORP and RARP, where the odds ratios of autologous and homologous transfusion use during RARP were about 1/25th and 1/7th, respectively, of those during ORP. Claims of a less invasive nature of RARP over ORP have been described in several publications.^(4–7) The results of the current study are noteworthy in that the favorable outcomes with RARP had been achieved at an early phase of the introduction of the technology. The shorter postoperative length of stay and lower cost excluding operation associated with RARP also supports the concept of less invasiveness and quicker recovery with RARP than with ORP or MIE-RP.

However, in terms of comparisons between RARP and LRP, several reviews and RCTs noted that the difference in perioperative outcomes between the two techniques was marginal. For example, three of four recent meta-analyses and both RCTs reported similar transfusion rates for RARP and LRP,^(2–8) whereas our data indicated significantly lower rates of complications and transfusions with RARP compared with those with LRP. One reasonable explanation was that this was a population-based study that included not only highly skillful facilities but also a wide variety of hospitals, which might more directly reflect the outcomes in real-world clinical practice.

Regarding the anesthesia time, RARP had the longest duration among the four types of radical prostatectomy, even though existing publications mainly reported similar or shorter operation times for RARP than for LRP.^(3,5,6,8) This difference is probably because many of our RARP surgeons were still only at the half-way point of their learning curve. Doumerc *et al.*⁽²⁶⁾ reported that experience with approximately 110 RARPs was required to achieve the proficiency of a 3-h operation time. However, we think that other favorable outcomes of RARP offset the negative feature of a long anesthesia time.

Finally, we cannot avoid the greatest disadvantage of RARP: its cost. Bolenz *et al.*⁽²⁷⁾ warned that the use of robot technology was increasing without a mature assessment of cost-effectiveness. In the present study, RARP was associated with a 52.7% increase in the total cost compared with ORP. This is an important disadvantage despite its low complication rate and shorter postoperative length of stay, and a justification of this heavy cost pressure on national universal health care insurance would be required in the near future. The cost differences are mainly explained by the official fee for the surgery itself: approximately \$4108 for ORP versus \$7743 for LRP versus \$5978 for MIE-RP versus \$9528 for RARP (as of April 2012). Another concern relating to cost is profitability. It is estimated that a single robotic console costs approximately \$1.5 million, and a dual-console is \$2.25 million. There is also an annual maintenance fee of \$150 000.^(27,28) Kuwahara⁽²⁹⁾ estimated that a Japanese hospital needs at least 100 RARP cases annually to balance the profit and loss equation. Considering that there were 12 992 radical prostatectomies in the 2012 DPC database and hearing that Japan would add more than 100 surgical robots, the question of profitability arose. However, because of limited available data, it is difficult to deepen the discussion about cost-effectiveness of RARP in the current study. The data in the present study, however, can contribute to the formation of health care policy involving the future management of surgical robot distribution in Japan.

Some limitations in the present study must be mentioned. First, it is a retrospective, observational study, and patients were not assigned to each radical prostatectomy group randomly but on clinical practice basis. Unobserved confounders could cause biased results, although we exerted our best efforts to reduce the potential bias by incorporating multiple imputation, propensity-score matching, and generalized estimating equations.^(15–19) Second, the DPC database lacked some highly interesting variables such as extent of lymph node dissection, nerve-sparing performance, blood loss volume, conversion to open surgery, and postoperative status in urinary incontinence and erectile dysfunction. Anesthesia time was used as one of the outcomes in the present study, however, real surgical time, which was not available from the DPC database, would be more ideal. Third, an administrative claims database might contain some inadequate coding, which could lead to underestimation or overestimation of events. Fourth,

hospitalization duration and cost data largely vary from one country to another, so the generalizability of our findings may be limited. Among developed countries, Japan is famous for its long length of stay.⁽³⁰⁾ Finally, the hospitals in the DPC database are not sampled randomly and are biased toward those with a large bed volume.⁽³¹⁾

Despite these limitations, our analyses provide up-to-date information for the safety aspect of RARP during the year of its initial introduction in Japan, which was worthwhile for robot-assisted surgery in any field.

In conclusion, the introduction of robotic surgery in Japan has led to dynamic changes in the clinical structure and outcomes of prostate cancer surgery. Based on the retrospective population-based analysis during its initial year, it was observed that RARP would be associated with several favorable safety aspects when compared with three conventional prostatectomies, although it would have the longest anesthesia time and was the most costly.

Disclosure Statement

The authors have no conflict of interest.

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Abbreviations

CCI	Charlson comorbidity index
DPC	Diagnosis Procedure Combination
ICD-10	International Classification of Diseases and Related Health Problems, 10th Revision
LRP	laparoscopic radical prostatectomy
MIE-RP	minimum incision endoscopic radical prostatectomy
ORP	open radical prostatectomy
RARP	robot-assisted radical prostatectomy
RCT	randomized control trial

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Supporting Information

Additional supporting information may be found in the online version of this article:

Table S1. Definitions of perioperative complications

Table S2. Detailed background and outcome data after multiple imputation and one-to-one propensity-score matching