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Effect of Postoperative Pain Management after Robot-Assisted Radical Prostatectomy: A Study on Reducing Hospital Length of Stay and Medical Costs Using Japanese Nationwide Database

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Prostate cancer has a high incidence rate. Many articles reported its usefulness with the advent of robotic surgery in 2001. However, epidural analgesia is declining due to the spread of minimally invasive treatment. There have been no studies using nationwide databases on the impact of epidural analgesia use on length of hospital stay and medical costs. Therefore, we used a Japanese national inpatient database from April 2016 to March 2020. The study population included 46,166 patients. We compared a postoperative analgesia management group using epidural analgesia [Epidural Analgesia Group (EA Group): 5,354] and a group not using epidural analgesia [non-Epidural Analgesia Group (non-EA Group): 40,812]. We found significant differences among the two groups regarding the length of stay, days from surgery to discharge, and inpatient cost of surgery to discharge. Hospital length of stay and postoperative hospital stay was statistically shorter in the EA group than in the non-EA group (11.3 ± 2.8 days vs. 12.1 ± 3.1 days, $p < 0.001$ and 8.9 ± 2.5 days vs. 9.3 ± 2.7 days, $p < 0.001$), respectively, and medical costs were also significantly lower in the EA group (84,566 JPY vs. 294,277 JPY, $p < 0.001$). Also, the activities of daily living (ADL) assessment at discharge determined a considerably higher score in the EA group than in the non-EA groups. Epidural analgesia for postoperative pain management largely depends on each medical institution's treatment policy. However, epidural analgesia is declining due to the spread of minimally invasive treatment. Therefore, epidural analgesia should be reconsidered because it can reduce hospital stays and hospitalization costs.

Keywords: diagnosis procedure combination database; hospital length of stay; postoperative pain management; prostate cancer; robot-assisted radical prostatectomy
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Introduction

Prostate cancer (PCa) is the most common cancer for Japanese men. PCa was about 18% of all cancers in 2020 (Cancer Today 2020a). Also, it is the second most common cancer in the world after lung cancer (Cancer Today 2020b). Surgical excision and radiation therapy are the standard treatments for localized PCa (Mitsunari et al. 2021). In Japan, health insurance covers four types of surgical excision: retropubic radical prostatectomy (RRP), laparoscopic radical prostatectomy (LRP), minimum incision endoscopic retropubic prostatectomy (MIPRP), and robot-assisted radical prostatectomy (RARP). In addition, health insurance covered RARP in 2012, rapidly becoming widespread. RARP accounted for 77% of surgical prostatectomies in 2019 and is now the standard procedure (Ministry of Health, Labour and Welfare 2019). Abbou et al. (2000) first reported RARP in 2000. Since then, it has rapidly spread, mainly in Europe and the United States. By December 2021, hospitals had installed 6,730 robotic surgical systems in 69 countries (Intuitive Surgical 2022; Japan Robotic Surgery Society 2022). In Japan, more than 249 acute care institutions used robotic surgery systems. In the past study on RARP, it has a shorter operator learning curve, lower

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perioperative complication rates, shorter hospital stays, and lower blood loss and transfusion risks compared to the other three surgeries (Frota et al. 2008; Basiri et al. 2018; Saika et al. 2018; Mitsunari et al. 2021). Laparoscopic surgery allows for a smaller surgical wound compared to open surgery. Past studies have shown the usefulness of epidural analgesia (EA) for postoperative pain management. However, its use has declined due to the widespread use of minimally invasive procedures that allow for a smaller surgical field (Hemmerling 2018; Zeltsman et al. 2020; Rawal 2021).

On the other hand, the length of hospital stay and the content of medical care varies widely from medical institution to medical institution. Today, with the current emphasis on encouraging early postoperative release and improving activities of daily living (ADL), nursing research is also being conducted from various perspectives (Shiba and Matsuda 2014; Ozawa and Kawahara 2017). However, no studies are using nationwide databases on the impact of EA use on length of hospital stay and medical costs. This study examined the effect of postoperative pain management with EA after RARP on early release from the bed, postoperative length of stay, and healthcare costs using Diagnosis Procedure Combination (DPC) data. Using a large data set, we aimed to compare the status of EA implementation in Japan in recent years and outcomes with the non-EA group.

Materials and Methods

Data source

DPC is a comprehensive per diem payment system based on diagnosis group classification for acute inpatient care managed by the Ministry of Health, Labour and Welfare (MHLW). More than 1,700 medical institutions and 54% of all general hospital beds are covered by the DPC (Ministry of Health, Labour and Welfare 2020). The DPC database stores medical fee billing data for the government. It includes basic patient information, diagnoses based on ICD-10 (International Statistical Classification of Diseases and Related Health Problems 10th Revision), comorbidities, length of hospital stay, the outcome at discharge, ADL scores at admission and discharge, and medical care provided during the hospitalization period with medical fee billing codes.

This study analyzed DPC data held by the DPC Research Institute. The data collected more than 7 million cases from over 1,100 hospitals annually. This data includes an analysis of the actual medical care conditions, costs, quality, and outcomes in acute care hospitals (Yasunaga 2019). In addition, analytical studies using this DPC data have been published from various perspectives. (Tarasawa et al. 2020; Fujimori et al. 2021a, b, c; Noda et al. 2021; Moroi et al. 2022) On the other hand, the Japanese National Data Base (NDB) is also managed by the MHLW. The National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) focused on the “Act on Securing Medical Care for the Elderly” that collects receipt information from insurers. The background was constructed as a resource for planning medical cost optimization. NDB aggregate data is available to the public as open data. Still, it does not include the details of the actual healthcare provision. The DPC data used in our study accounted for approximately 70% of the NDB data.

The Ethics Committee has approved this study of the Tohoku University Graduate School of Medicine (No. 2021-1-1082). The subject data have been anonymized, so informed consent is not required.

Patient selection

The study covered four years, from April 2016 to March 2020. RRP, LRP, MIERP, and RARP surgeries performed on patients who fall under C61 (Prostate Cancer) of ICD-10 were extracted from the DPC database. After figuring out the total PCa surgery, RRP, LRP, and MIERP were removed. Patients hospitalized for more than 30 days were excluded because the DPC has a specific length of stay for each diagnosis grouping. For example, the length of stay in RARP is up to 30 days. To avoid the effects of surgical invasions other than RARP, patients who underwent surgery after RARP were also excluded. Finally, patients were divided into two groups: (the EA group and the non-EA group).

Data collection

This study obtained basic patient information from the Form 1 file. This file includes age, body mass index (BMI), length of hospital stay, postoperative length of hospital stay, TNM classification, inpatient ADL, and outpatient ADL performed at a university hospital. All data compared the EA and non-EA groups. EA was performed using the reimbursement billing code of L003. L003 is a billing code for continuous local anesthetic infusion after epidural anesthesia and can be calculated daily.

We extracted the details of provided medical care during hospitalization from the F-files. This file incorporates the details of medical treatment, including extracted anesthesia time, blood transfusion, number of days of urinary catheter placement, and postoperative hospitalization costs. In addition, EA extracted postoperative analgesic management and intravenous acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs). Finally, we calculated the percentage of analgesic medications used. The use of EA has decreased due to the increase in minimally invasive procedures, multi-model analgesia, rising awareness of perioperative thromboembolism prevention, and calculating the performed rate of EA by the institution from hospital codes.

Statistical analysis

This study used means and standard deviations for continuous variables such as age, BMI, length of hospital stay, postoperative stay, and anesthesia time. In addition, percentages are shown for categorical data such as stage T and N cancer classification and drug use. Welch's t-test, χ^2 test, simple linear regression, and multilevel analysis were used for statistical analysis. For the multilevel analysis, we used the two-level structure comprised patient and hospital-level factors. The following outcomes were analyzed using multilevel regression models with the same two-level structure: days from surgery to discharge and inpatient cost from surgery to discharge. The models included the age, BMI, Barthel Index at inpatient, and hospital surgery case volume as confounding factors. In all cases, two-sided significance probabilities were set at < 0.05. IBM SPSS Version 28.0.0.0 for Windows (IBM Corp., Armonk, NY, USA) was used as the analysis software.

Results

Fig. 1 shows the patient selection process in this study. First, we selected 66,574 surgical patients from the 451,186 prostate cancer patients database. Then, we excluded RRP, LRP, MIERP surgeries, hospital stays over 30 days, and other surgeries performed after RARP. We used 46,166 RARP patients' data as 5,354 in the EA group and 40,812 in the non-EA group.

Table 1 shows the number of prostate surgeries in DPC Database from April 2016 to March 2020. During this period, there were 10,071 RRP cases, 7,536 LRP cases, 2,021 MIERP cases, and 47,218 RARP cases. Compared to NDB, the 47,218 RARP patients in the DPC database represent 74% of the 63,681 RARP patients enrolled in the NDB. The number of PCa surgeries is on an upward trend in Japan, as registered by the NDB. Also, RRP is decreasing while RARP has been increasing in recent years in Japan. (Ministry of Health, Labour and Welfare 2016, 2017, 2018a, 2019)

Table 2 shows basic patient information. We found no significant differences between the two groups in age and BMI (p = 0.127 and 0.280). We converted the ten items of

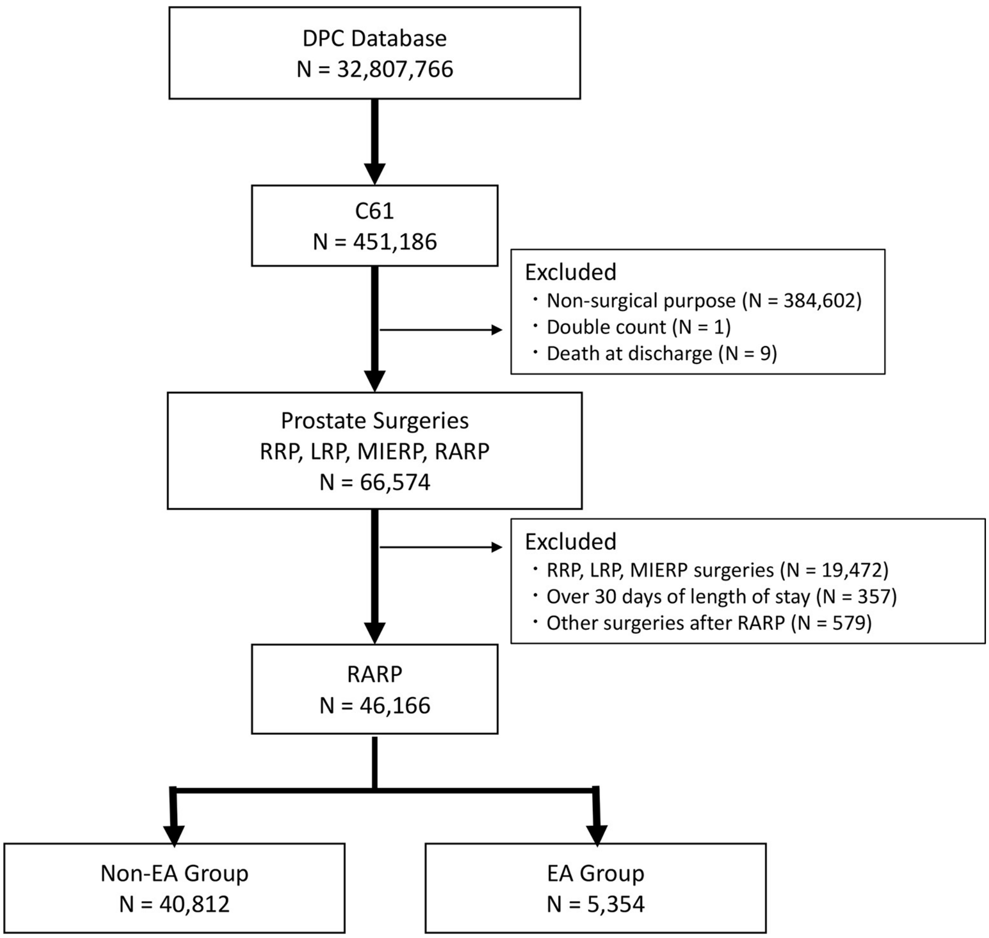

Fig. 1. Patients selection flow chart.
The Diagnosis Procedure Combination (DPC) database contains more than 32 million patients from April 2016 to March 2020. We extracted 66,574 surgical patients from this database out of 451,186 prostate cancer patients. Of the surgical patients, 46,166 patients who underwent robotic surgery were classified into two groups: 5,354 patients who used epidural analgesia (EA) postoperatively, and 40,812 patients who did not. In addition, we selected three procedures other than robotic surgery to examine the number of prostate cancer surgeries in recent years.
C61, the billable ICD-code used to specify a diagnosis of prostate cancer; RRP, retropubic radical prostatectomy; LRP, laparoscopic radical prostatectomy; MIERP, minimum incision endoscopic retropubic prostatectomy; RARP, robot-assisted radical prostatectomy.

Table 1. Number of prostatectomy in the Diagnosis Procedure Combination (DPC) database.

Data period	RRP	LRP	MIERP	RARP	Total
April 2016 ~ March 2017	3,893 (22.5)	1,984 (11.5)	657 (3.8)	10,733 (62.2)	17,267
April 2017 ~ March 2018	2,613 (15.8)	1,893 (11.5)	433 (2.6)	11,564 (70.1)	16,503
April 2018 ~ March 2019	2,074 (12.3)	1,949 (11.5)	495 (2.9)	12,407 (73.3)	16,925
April 2019 ~ March 2020	1,491 (9.2)	1,710 (10.6)	436 (2.7)	12,514 (77.5)	16,151

Number of prostate cancer surgeries performed in a year is shown with percentages of total in parenthesis.
RRP, retropubic radical prostatectomy; LRP, laparoscopic radical prostatectomy; MIERP, minimum incision endoscopic retropubic prostatectomy; RARP, robot assisted retropubic prostatectomy.

Table 2. Patient demography.

		Non-EA Group (N = 40,812)		EA Group (N = 5,354)		p value
		mean or N	(SD) or %	mean or N	(SD) or %	
Patient factors						
Age, Years, mean (SD)		68.2	(6.1)	68.1	(5.8)	0.127
BMI, kg/m^2, mean (SD)		24.0	(3.5)	24.1	(3.0)	0.280
Barthel Index at inpatient, score, mean (SD)		99.4	(7)	99.8	(3.1)	0.022
Stage_T	T0	73	0.2	28	0.5	< 0.001
	T1	8,302	20.3	824	15.4	< 0.001
	T2	22,953	56.2	3,210	60.0	< 0.001
	T3	4,291	10.5	628	11.7	0.007
	T4	120	0.3	13	0.2	0.511
	TX	5,073	12.4	651	12.2	0.572
Stage_N	N0	35,668	87.4	4,625	86.4	0.037
	N1	476	1.2	47	0.9	0.061
	N2	8	0.0	0	0.0	0.306
	N3	1	0.0	0	0.0	0.717
	NX	4,659	11.4	682	12.7	0.004
Hospital Factors (249 institutions)						
Surgery cases of RARP						
Low (0~71)		1,549	3.8	387	7.2	< 0.001
Medium (72~166)		5,915	14.5	1,493	27.9	< 0.001
High (167~260)		11,686	28.6	1,451	27.1	0.019
Very High (261~846)		21,662	53.1	2,023	37.8	< 0.001
Academic hospital		18,662	45.7	1,153	21.5	< 0.001

Values are shown as mean (standard deviation, SD), or numbers of subjects per group with percentages. Hospital surgery case volume of RARP was divided into four quartiles; low, medium, high and very high. Welch's t-test was used for the statistical analysis of age, BMI, and Barthel Index at inpatient. χ^2 test was used for the statistical analysis of Stage T, N, surgery cases of RARP and academic hospital.
EA, epidural analgesia; BMI, body mass index; RARP, robot-assisted radical prostatectomy.

inpatient ADL assessment into the Barthel Index, and we compared the two groups. The mean Barthel Index score for both groups was above 99 points, and significant differences were found ($p = 0.022$). The highest cancer stage was T2 for non-EA and EA, accounting for 56.2% and 60%, respectively. The results showed significant differences in T0, T1, and T2 stages ($p < 0.001$). The stage of lymph node metastasis was N0 in more than 85% of the patients in each group ($p = 0.037$).

Table 3 shows the patient outcomes difference between EA and non-EA. The hospital length of stay and days from surgery to discharge was significantly shorter in the EA group than in the non-EA group ($p < 0.001$). Also, the Barthel Index score at discharge was statistically higher in the EA group than in the non-EA group ($p < 0.001$). The EA group's anesthesia time was 7 minutes longer ($p < 0.001$). Blood transfusions were performed less than 1% in both groups. These differences were significant ($p = 0.043$). Postoperative hospitalization costs were statistically 9,711 yen lower in the EA group than in the non- EA group (p <

Table 3. Difference between EA and non-EA Groups.

	Non-EA Group (N = 40,812)		EA Group (N = 5,354)		p value
	mean or N	(SD) or %	mean or N	(SD) or %	
Hospital length of stay, days, mean (SD)	12.1	(3.1)	11.3	(2.8)	< 0.001
Days from surgery to discharge, days, mean (SD)	9.3	(2.7)	8.9	(2.5)	< 0.001
Barthel Index at discharge, score, mean (SD)	98.4	(11.3)	99.6	(3.9)	< 0.001
Anesthesia time, min, mean (SD)	303.9	(80.6)	311.2	(77.2)	< 0.001
Blood transfusion	335	0.8	30	0.6	0.043
Urinary catheter day, days, mean (SD)	6.6	2.2	6.5	2.0	< 0.001
Inpatient cost from surgery to discharge					
JPY, mean (SD)	294,277	(87,724)	284,566	(76,750)	< 0.001
Post operative pain medications					
Acetaminophen	29,097	71.3	2,586	48.3	< 0.001
NSAIDs	18,132	44.4	2,142	40.0	< 0.001
Acetaminophen + NSAIDs	12,418	30.4	1,074	20.1	< 0.001
non-pain controls	6,001	14.7	1,700	31.8	< 0.001

Values are shown as mean (standard deviation, SD), or numbers of subjects per group with percentages. Welch's t-test was used for the statistical analysis of hospital length of stay, days from surgery to discharge, Barthel Index at discharge, anesthesia time, urinary catheter days, and inpatient cost from surgery to discharge. χ^2 test was used for the statistical analysis of blood transfusion and postoperative pain medications.
EA, epidural analgesia; NSAIDs, non-steroidal anti-inflammatory drugs.

Table 4. Simple and multilevel analysis for post-operating length of stay and inpatient costs of patients.

	Simple linear regression			Multilevel linear regression		
	Coefficient	95% CI	p value	Coefficient	95% CI	p value
Days from surgery to discharge (days)						
non-EA Group	reference			reference		
EA Group	−0.398	−0.475 to −0.321	< 0.001	−0.019	−0.152 to 0.114	0.781
Inpatient cost from surgery to discharge (JPY)						
non-EA Group	reference			reference		
EA Group	−9,710	−12,175 to −7,244	< 0.001	1,203	−2,756 to 5,645	0.500

Estimated by a multilevel regression model after adjusting for the age, BMI, Barthel Index at inpatient, epidural analgesia, and hospital surgery case volumes.
EA, epidural analgesia; CI, confidence interval.

0.001). We compared analgesic medication between the EA and non-EA groups for intravenous administration with acetaminophen, medication with NSAIDs, or a combination of both. The percentage of postoperative analgesic use was statistically lower in the EA group than in the non-EA group ($p < 0.001$).

Table 4 shows linear regression analysis for days from surgery to discharge and inpatient cost from surgery to discharge. Simple linear regression showed that the EA group had significant decreases in days from surgery to discharge and in inpatient cost from surgery to discharge (coefficient: –0.398 days, 95% CI; –0.475 to –0.321, $p < 0.001$ and coefficient: –9,710 JPY, 95% CI; –12,175 to –7,244, $p < 0.001$, respectively). However, when we used a multilevel analysis, the significant difference between the two groups disappeared in both cases (coefficient: –0.019 days, 95% CI; –0.152 to 0.114, $p = 0.781$ and coefficient: 1,203 JPY, 95% CI; –2,756 to 5,645, $p = 0.500$, respectively). Before used multilevel analysis, we compared a null model with a model that facility factors for check the intra-class correlation coefficient (ICC). The ICC is the variance between medical facilities divided by the total variance, and the ICC in this model was 0.296. And the variance between facilities using Wald's Z-values was 10.7 and statistically significant.

Fig. 2 shows the percentage of EA performed by each medical institution. The DPC data includes medical institution codes and can be aggregated by the medical institution. In this study, 249 medical institutions conducted RARP. The breakdown of 249 facilities was five institutions administrated EA in all cases, and 22 institutions provided more than 90% of the cases. On the other hand, 197 institutions

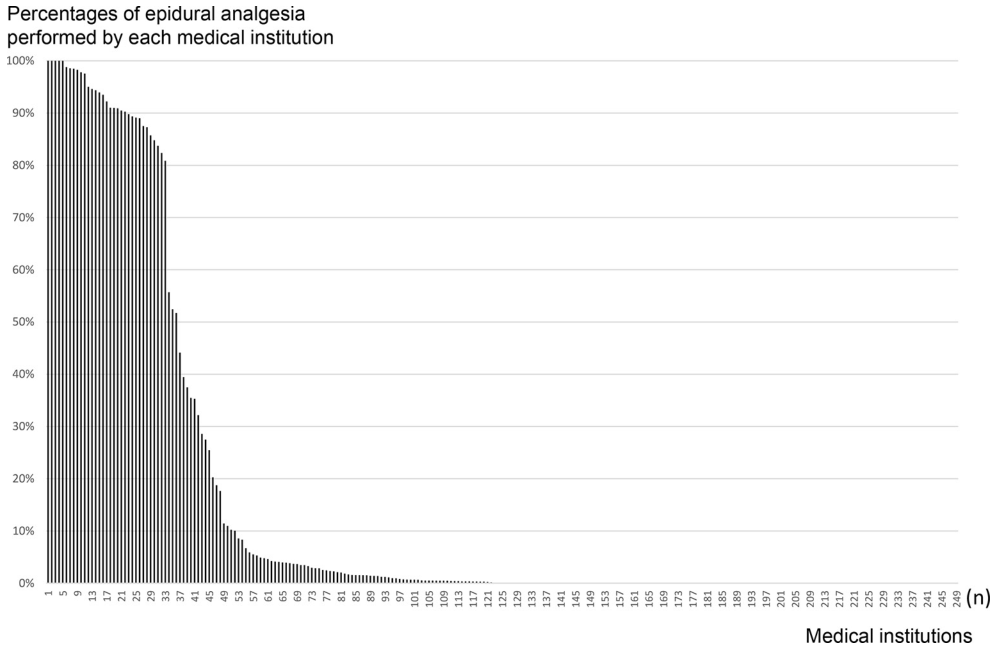

Fig. 2. Percentages of epidural analgesia (EA) for robot-assisted radical prostatectomy (RARP) performed in each institution. The study covered 249 facilities that had implemented RARP. The EA implementation rate for each medical facility was calculated and listed in order of highest implementation rate.

Table 5. Percentages of epidural analgesia performed in a year.

	*Institution (%)	Case (%)
April 2016 ~ March 2017	28.0	11.9
April 2017 ~ March 2018	34.9	12.2
April 2018 ~ March 2019	31.8	10.7
April 2019 ~ March 2020	33.2	11.6

Data were shown as percentages of efficacy rate of epidural analgesia.
*Calculated with an epidural analgesia implementation rate of at least 10%.

had less than 10% or non-EA rates. The graph also shows that most medical institutions do not conduct EA.

Table 5 shows the EA implementation rates from 2016 to 2019 in medical institutions that implemented at least 10% of EA. The number of EA performed by medical institutions was around 30%. The total number of performed EA was around 10%. There was no change over the four years, with repeated increases and decreases, but no downward trend.

Discussion

This study used 72% of RARP's NDB data of 63,681 cases, which can explain the current status of PCa surgery in Japan. In addition, over 24,000 reported articles on robotic surgery are in the literature. (Intuitive Surgical 2022). The articles compare conventional techniques, advantages, and disadvantages of robotic surgery, and review the initial implementation and cost comparisons. Our perspectives on postoperative analgesia management and combining hospital stay and medical costs with EA as the axis led to new findings.

We found that postoperative analgesia with EA decreased hospital stays by 0.4 day and postoperative inpatient costs by about 10,000 JPY. Furthermore, inpatient and discharge ADL comparisons showed significantly higher Barthel Index scores in the EA group. Since robotic surgery is performed in acute care facilities, it is necessary to discharge patients as soon as possible and return them to society. Therefore, from our findings, using EA is beneficial in medical cost optimization. EA has also been reported to have benefits leading to early release and early discharge (Suzuki 2014). Based on past research, EA promotes ADL recovery by appropriately controlling pain, facilitating early weaning, allowing patients to eat without inhibiting intestinal peristalsis, and potentially reducing hospital stay.

Robotic-assisted surgery is becoming the mainstream for PCa surgery, mainly in developed countries. It accounts for over 70% of prostate cancer surgeries in Japan. Robotic surgery is also expanding its adapted beyond the prostate to include the kidney, stomach, uterus, lungs, and heart (Ministry of Health, Labour and Welfare 2018b). On the other hand, not all medical institutions have adopted robotic surgery because of the high cost of installing and maintaining the equipment (Kajiwara et al. 2018). Therefore, robotic surgery has been introduced mainly at core hospitals in the region. Robotic surgery also requires surgical team training involving nurses and medical engineers. Medical institutions that perform robotic surgery in urology will improve occupancy and cost-effectiveness by enabling their teams into other surgical procedures (Stewart et al. 2019).

Today, as conventional and robotic surgeries are replacing each other, we can assume that patients are increasingly concentrated in hospitals that perform robotic surgeries (Tsukamoto and Tanaka 2016; Sugihara et al. 2017). This finding can be considered to facilitate the differentiation of hospital functions.

In addition to EA, abortive medications, intravenous medications, peripheral nerve blocks, and other methods of postoperative pain management are widely used. Multimodel analgesia, which compensates for the shortcomings of each analgesic method rather than providing pain management in isolation, is essential (Tubog 2021). Previous studies have reported that postoperative analgesia with EA for RRP prolongs the length of hospital stay (Mir et al. 2013). In addition, EA has been reported to have several advantages, including the ability to adjust the spread of the drug to the target site, superior analgesia during body movement, early release, fewer respiratory complications such as atelectasis, and no suppression of peristalsis of the digestive tract (Suzuki 2014). On the other hand, EA has serious complications such as epidural blood or an epidural abscess caused by the catheter (Yokoyama 2009; Makito et al. 2021). However, complications are infrequent, occurring in 1 in 190,000 cases according to a large-scale study (Wulf 1996).

Furthermore, studies comparing the effects of acetaminophen and NSAIDs suggest that acetaminophen administration is preferable to NSAIDs in RRP. Still, the dosage and frequency per dose should be increased if the pain is severe (Nishimura et al. 2021). The analysis of medication status as postoperative pain management showed no difference between the EA and non-EA groups. Therefore, we inferred the advantages and disadvantages of each method complemented each other in analgesia management.

Finally, the decision to implement an EA may depend on the clinical path developed by each medical institution. Since medical facility factors are expected to affect outcomes, a multilevel analysis was performed, and the intraclass correlation coefficient (ICC) value was also 0.3, indicating the influence of medical facility factors. In addition, a multilevel analysis of patient - medical institution did not show any significant difference, indicating no reduction in either length of hospital stay or medical costs. Therefore, we can consider that the clinical path and characteristic of medical institutions is a factor that influences the length of hospital stay. The utility of EA should be recognized as being able to shorten the length of hospital stay by even half a day and to discharge patients in better condition in terms of ADL values. Also, EA is contraindicated in patients with abnormal hemostasis and coagulation, cerebral hypertension, extreme hypotension, and spinal abnormalities. Therefore, it is assumed that EA could not be performed on a certain number of patients. Of the data obtained in this study, an implementation rate of more than 50% is 36 institutions, which was only 14% of all institutions. Although Fig. 2 clearly shows that more than half of the medical institutions do not use EA, EA still has the potential to shorten the length of postoperative hospital stay. A shorter hospital stay is expected to lower medical costs. Therefore, we determined that hospitals could reconsider the use of EA.

There are two points of concern, and we must consider limitations in interpreting the current results. First, pain perception varies significantly from person to person. The DPC does not have data such as NRS (Numerical Rating Scale), VAS (Visual Analogue Scale), and FPS (Face Pain Scale) to determine the state of pain felt by patients. Thus, appropriate pain assessment is not possible. Therefore, the status of analgesic prescriptions according to pain level is unclear. In particular, a prophylactic prescription may be prescribed as an abortive medication. Second, further studies should investigate the duration of analgesic treatment. In the DPC, the dosage of oral medications may not match the actual number of days of use, and the relationship to pain management is unclear. This is because prescriptions for oral medications are compiled on the first day of medication administration, and the DPC data does not reflect when and how much was used.

In conclusion, PCa surgeries have increased recently, and RARP has replaced the procedure from RRP. RARP covered 77.5% of all PCa surgeries in 2019. In addition, the study revealed that EA could shorten postoperative hospital stay and may contribute to reducing postoperative hospitalization costs. Although EA was used in only 11.5% of all cases and varied widely from institution to institution, the use of EA is possibly reconsidered for postoperative pain management.

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Conflict of Interest

The authors declare no conflict of interest.

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