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Original Article

Optimal interval for delayed retrieval surgery with reciprocating morcellators after enucleation of giant prostatic hyperplasia in holmium laser enucleation of the prostate

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Abstract *Objective:* The aim of this research was to evaluate the efficiency of reciprocating morcellation for removing giant benign prostatic hyperplasia during holmium laser enucleation of the prostate, investigate whether performing morcellation as a two-stage procedure improves tissue retrieval efficiency, and seek to determine the optimal interval between the two surgeries.

Methods: This study included nine cases of holmium laser enucleation of the prostate with an enucleated prostate weight exceeding 200 g, indicative of substantial prostate enlargement. Morcellation was performed on Day 0 (n=4), Day 4 (n=1), Day 6 (n=1), and Day 7 (n=3). The intervals were compared regarding the morcellation efficiency, beach ball presence, and pathology.

Results: The mean estimated prostate volume was 383 (range 330–528) mL; the median enucleation weight was 252 (interquartile range [IQR] 222, 342) g; and the median enucleation time was 83 (IQR 62, 100) min. The mean morcellation efficiency was 1.44 (SD 0.55) g/min on Day 0 and 13.69 (SD 2.46) g/min on day 7. The morcellation efficiency was 4.15 g/min and 10.50 g/min on Day 4 and Day 6, respectively, with significantly higher in the two-stage group compared to one-stage group (11.0 g/min *vs.* 1.5 g/min; p=0.014). Efficiency was strongly correlated with intervals (p<0.001); the incidences of beach balls were 100% (4/4) and 60% (3/5) in the immediate and two-stage surgery groups, respectively.

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Conclusion: The efficiency of two-stage morcellation with reciprocating morcellators was highly related to the postoperative interval, with the maximum efficiency reached on Day 7.

1. Introduction

1.1. Holmium laser enucleation of the prostate (HoLEP) as a size-independent surgery for benign prostatic hyperplasia

HoLEP is one of the treatment options recommended by the American Urological Association for a very large prostate (*i.e.*, >150 mL) with no specified upper limit of size [1]. In real-world practice, occasionally patients present with giant prostates (>500 mL) [2]. For giant adenomas, HoLEP mainly focuses on enucleation, which can be completed in up to 2 h by an experienced surgeon, regardless of the size [3].

1.2. Morcellation problems in HoLEP for giant prostates

Morcellator retrieval efficiency does not vary and the time required for morcellation is in proportion to the prostate size. Currently morcellator types used include oscillation (Piranha, Richard Wolf, Knittlingen, Germany; DrillCut, Karl Storz, Tuttlingen, Germany) and reciprocation (VersaCut, Lumenis, Palo Alto, CA, USA). A systematic review reported respective retrieval efficiencies of 5.29 g/min, 5.3 g/min, and 3.95 g/min, respectively, for these three morcellators [4].

Although the reciprocating morcellator is used almost dominantly in Japan, it has a significantly lower collection efficiency for extremely large prostates [3] and higher incidence of round and dense nodules, called the beach ball (BB), which is difficult to aspirate, compared to the other morcellators [5]. Although HoLEP is associated with less blood loss compared to other surgeries and does not cause hyponatremia, complications (such as hypothermia and shivering) may occur during prolonged surgery [6]. The duration of surgery may determine the prostate volume treatable with HoLEP.

Therefore, open techniques for tissue retrieval are sometimes used for giant adenomas [7]. However, we prefer to complete the endoscopic procedure via two-stage morcellation. Although two-stage morcellation increases the retrieval efficiency due to tissue softening, no previous studies have investigated the change in retrieval efficiency according to the interval between surgeries.

In this study, we investigated the morcellation efficiency and surgical interval in cases with giant adenomas (>200 g) treated with HoLEP. In addition, the pathological changes and presence of BBs in delayed cases, as well as the optimum surgical interval, were investigated.

2. Patients and methods

2.1. Participants and surgical procedures (enucleation)

This study was approved by the Ethical Review Committee of St. Luke's International Hospital (approval number: 22-R004). In total, nine out of 1436 HoLEP cases with an enucleation weight of >200 g, operated on at the Department of Urology, St. Luke's International Hospital, between September 2011 and March 2021 were included in this study. The study was conducted retrospectively and the need to obtain written informed consents from the patients was exempted by the Institutional Review Board. Personal identifiers of the patients were removed, and the data were analyzed anonymously.

The surgery was performed by the senior physician (Endo F) or under his supervision. The endoscope used was manufactured by Storz (Tuttlingen, Germany), and enucleation was performed using a Lumenis Versapulse laser generator (Lumenis, Yokneam, Israel) with an output setting of 2.6 J×30 Hz in a short pulse. Enucleation was performed using the 2-lobe or 3-lobe technique based on the anteroposterior dissection HoLEP [8]. After enucleation, all patients underwent complete hemostasis with transurethral electro-fulguration. Using the Lumenis VersaCut morcellator (Lumenis, Palo Alto, CA, USA), tissue was collected in the bladder instead of the prostate fossa using the inversion method [9]. When BBs were encountered, they were either extracted with grasping forceps or retrieved by cutting with a transurethral resection. The irrigation solution was saline solution at room temperature (approximately 22 °C), not heated according to Joint Commission International criteria [10].

2.2. Surgical procedures (morcellation)

In this case series, the first two cases were planned as one-stage surgeries. The subsequent three cases were planned as two-stage surgeries. For cases beyond the fifth, we used preoperative MRI to estimate the enucleation and morcellation times. If the estimated surgical time exceeded 4 h, we opted for a two-stage surgery.

In the case of two-stage surgery, a catheter was placed after enucleation and the patient remained in the hospital until the second surgery. Two-stage morcellation was performed under general anesthesia and the catheter was removed 1–2 days after surgery. The patients were discharged after confirming normal urination.

2.3. Statistical analysis

We analyzed the interval between surgeries in terms of morcellation efficiency, the occurrence of BBs, pathological findings, and perioperative complications. Analyses were performed using Wilcoxon's rank sum test for continuous variables and Fisher's exact test for categorical variables. R software (version 4.0.3; R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis. The p-value of <0.05 was considered significant.

3. Results

Table 1 presents the characteristics of the nine cases with enucleation weights of >200 g included in the study. The mean estimated prostate volume was 383 (range 330—528) mL; the median enucleation weight was 252 (IQR 222, 342) g; and the median enucleation time was 83 (IQR 62, 100) min. In case #2, the prostate of 342 g was enucleated in 62 min, but the procedure was interrupted after a total operating time of 348 min due to hypothermia (33.8 °C) during morcellation. After 7 days, the residual adenoma was retrieved during a two-stage morcellation, with 171 g of previously enucleated tissue morcellated in 14 min.

In the subsequent seven cases, five patients had a two-stage surgery with morcellation on Day 7 in three cases (cases #3, #4, and #7), Day 4 in one case (case #5), and Day 6 in one case (case #9); and two cases (cases #6 and #8) were planned for one-stage surgery and were completed.

The relationship between morcellation efficiency and surgical interval was evaluated for nine cases. For case #2, data on the first morcellation were used for analysis.

The mean enucleation time was 80.7 (standard deviation [SD] 22.3; range 41—104) min and the enucleation efficiency was 3.9 (SD 1.9; range 2.2—6.7) g/min; the efficiency remained within a stable range in all cases. The morcellation efficiency data are presented in Fig. 1 and Table 2. The mean morcellation efficiency was 1.44 (SD 0.55) g/min on Day 0 and 13.69 (SD 2.46) g/min on Day 7. The morcellation efficiency was 4.15 g/min and 10.50 g/min on Day 4 and Day 6, respectively. The mean efficiency was significantly higher in the second compared to the first stage (11.0 g/min *vs.* 1.5 g/min; $p=0.014$) and strongly correlated with the number of days ($y=1.685x+1.027$, $r^2=0.899$, $p<0.001$).

For case # 2, who underwent two morcellations, a 16-fold increase in efficiency was seen from the immediate to 7-day timepoint (0.8 g/min and 12.2 g/min, respectively).

The incidences of BBs were 100% (4/4) and 60% (3/5) in the immediate and two-stage surgery groups, respectively, with a slightly lower incidence of 33% (1/3) on Day 7. The remaining BBs had to be removed using other devices, such as grasping forceps or by transurethral resection. The pathological examination showed that the epithelial cell component was necrotic and detached in all delayed cases, making diagnosis impossible (Fig. 2).

The catheter remained in place until the two-stage morcellation was completed. Postoperative hospital stay was markedly prolonged, 7 days for the one-stage surgery and 10 days for the two-stage surgery ($p=0.048$). The postoperative decrease in hemoglobin was not significantly different between the first and second stages of surgery (−3.1 g/dL and −2.3 g/dL, respectively; $p=0.462$). No blood transfusions were performed in this case series. One case who underwent two-stage morcellation surgery developed fever postoperatively, but quickly recovered without sepsis (Clavien—Dindo Grade II). Case #3 complained of mild pain associated with a massive enucleated adenoma (432 g) and catheter cuff in the bladder, which was resolved with analgesics. The median urinary incontinence (<1 pad/day) recovery time was 3 months, and was not significantly different between one- and two-stage surgeries ($p=0.617$).

4. Discussion

4.1. Prevalence of giant prostate hyperplasia

Prostate enlargement to >100 mL is observed in only 4% of men aged >70 years, but the actual number of patients with this condition is likely to be higher [11]. A giant

Table 1 Patients' background and surgical results.

Parameter	One-stage surgery ($n=4$)	Two-stage surgery ($n=5$)	p-Value
Age, year	77.5 (73.5, 78.5)	77.0 (72.0, 81.0)	0.902
Body mass index, kg/m^2	23.5 (23.0, 24.1)	24.4 (24.2, 25.1)	0.221
Estimated prostate volume, mean (range), mL	373 (354—402)	391 (330—528)	1.000
Prostate-specific antigen, ng/mL	12.5 (6.3, 19.7)	8.2 (7.4, 9.7)	0.807
Total operating time, min	344 (266, 363)	155 (132, 155)	0.014
Enucleation time, min	80 (52, 99)	83 (74, 102)	0.389
Enucleated weight, g	228 (197, 255)	252 (220, 361)	0.462
Change in hemoglobin, g/dL	−3.1 (−3.8, −2.0)	−2.3 (−3.6, −1.1)	0.462
Hypothermia (<34 °C), n (%)	2 (50)	0 (0)	0.167
Continent recovery, mean (range), month	2.5 (1—3)	5.5 (1—15)[a]	0.617
Hospital length of stay, day	6.5 (5.0, 8.0)	10 (9, 11)	0.048
Morcellation efficiency, g/min	1.5 (1.0, 1.9)	11.0 (10.5, 14.4)	0.014

Note: values are presented as median (interquartile range) unless stated otherwise.
[a] Data on continence recovery were missing in one case of two-stage surgery.

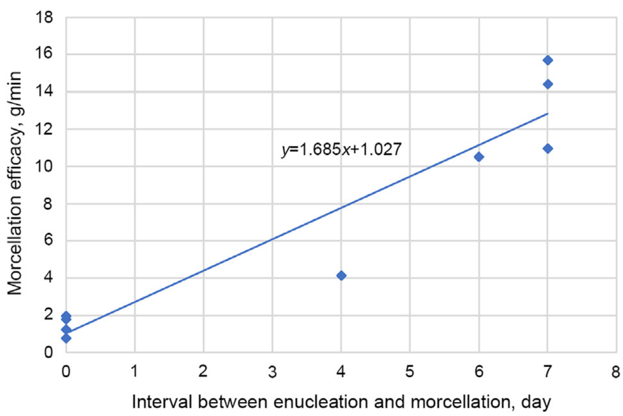

Figure 1 Relationship between morcellation efficiency and surgical interval. The morcellation efficiency was strongly correlated with the number of days. For case #2, data on the first morcellation were used for analysis.

prostate gland (>200 mL) [11] is sometimes encountered in clinical practice and there have been several reports of prostate glands of >700 g [12]. The largest prostate gland reported to date was of 3987 mL [13], and more than 500 mL of prostate can be encountered, even though this is rare.

Although HoLEP is the size-independent gold standard treatment for prostate enlargement [14], few studies have examined the suitability of different treatments according to prostate size. One previous case report described successful HoLEP for a giant enlarged prostate of 400 mL [15], but few systematic studies have been performed.

4.2. The case series of giant prostates treated with HoLEP

Recently, Zell et al. [3] reported the largest case series (88 cases) of HoLEP for patients with giant prostates (estimated volume of >200 mL). The study included 76 patients with prostate volumes of 200—299 mL (the smaller group) and 12 with volumes of >300 mL (the larger group) [3].

The efficiency of enucleation was significantly higher in the large than the small prostate group (2.6 mL/min *vs.* 2.0 mL/min, $p=0.04$), although the total enucleation times were similar and not significantly differ (82 min *vs.* 77 min) [3].

The study highlighted significant challenges in morcellation for larger prostates. The morcellation time increased significantly with increasing prostate size (46.8 min in the small group *vs.* 74.5 min in the large group; $p=0.021$) [3]. Reciprocating morcellators, used in 45 early-stage cases, were less efficient and presented more difficulties compared to oscillating morcellators, used in 34 late-stage cases. The oscillating morcellator demonstrated a higher retrieval efficiency (4.7 g/min *vs.* 3.3 g/min, $p=0.0006$) [3]. In larger prostates, the efficiency of retrieval decreased further with reciprocating morcellators (71.4% lower in the larger group) compared to oscillating morcellators (26.5% lower in the larger group). Seven cases using reciprocating morcellators required conversion to laparotomy due to visual field issues, and morcellation was aborted and converted to a second stage in 15 cases. Blood transfusions were necessary in 19.3% of cases, indicating the complexity and risks of HoLEP for prostates larger than 200 mL [3].

4.3. Reciprocating morcellation in giant prostates: our challenges

This number was comparable to that of the Zell et al.'s series [3]. The mean enucleation time and removal efficiency of our giant prostates were 80.7 min and 3.9 g/min, respectively, thus comparable to those of previous reports. Successful enucleation is possible for prostate sizes up to almost 500 mL [3].

However, the use of reciprocating morcellators resulted in lower recovery rates for extremely large prostates, such as those of >300 mL [3] and high incidence of BBs [4], leading to longer operative times. Since the enucleation time remained almost constant regardless of size, morcellation time was considered to be the most important factor in the operative time.

Initially, we planned HoLEP as one-stage surgery, but the first and second cases developed hypothermia (body temperature of <34 °C) almost 6 h after surgery. For case #2, the anesthesiologist requested termination of the operation. Transurethral surgery, especially HoLEP, results in hypothermia over time due to the use of a large quantity of irrigation fluid to fill the bladder during morcellation [6]. Jun et al. [6] reported a 1.3 °C decrease in deep body

Table 2 Surgical parameters and the presence of beach balls.

Case	Interval to morcellation, day	Enucleated weigh, g	Enucleation time, min	Enucleation efficiency, g/min	Morcellation time, min	Morcellation efficiency, g/min	Beach ball
1	0	222	100	2.22	180	1.23	Present
2	0	171	62	5.52	226	0.76	Present
	7	171	—	—	14	12.21	None
3	7	432	74	5.84	30	14.40	None
4	7	220	102	2.16	14	15.71	Present
5	4	361	62	5.82	87	4.15	Present
6	0	234	98	2.39	131	1.79	Present
7	7	252	104	2.42	23	10.96	None
8	0	276	41	6.73	140	1.97	Present
9	6	210	83	2.53	20	10.50	Present

—, not available.

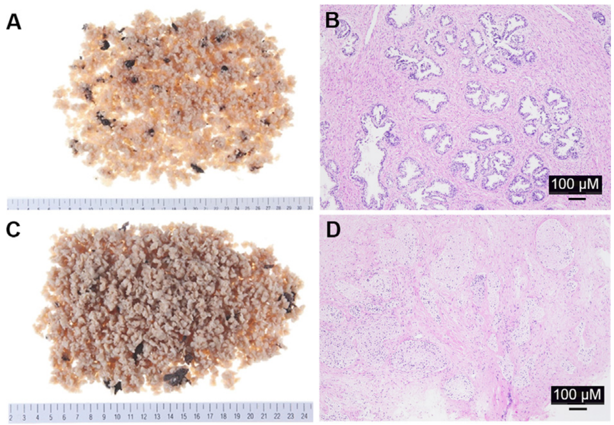

Figure 2 Pathological findings after surgery in case #2, in which surgery was interrupted due to hypothermia and two morcellation procedures were performed. (A and B) Immediately after surgery: gross appearance following fixation (A) and microscopic findings with hematoxylin and eosin staining (B); (C and D) Day 7 after surgery: gross appearance following fixation (C) and microscopic findings with hematoxylin and eosin staining (D). There was little change in appearance immediately and on Day 7, but microscopic findings showed that epithelial cells were degraded by necrosis in the delayed specimens.

temperature after 120 min of HoLEP, resulting in an increased frequency of hypothermia and shivering. The morcellation time may exceed 6 h in cases of giant prostatic hypertrophy, and hypothermia may affect the operative time.

Absorption of perfusate during enucleation may also be a possible cause of hypothermia, but no symptoms associated with increased fluid were present in this study, rendering the association unclear [16].

To avoid prolonged morcellation, we chose a two-stage morcellation approach for tissue retrieval, which increased the mean recovery efficiency over nine-fold to 13.69 g/min on the seventh day compared to 1.44 g/min immediately post-enucleation. This accelerated recovery applies even to larger prostates.

Pathological findings for tissue recovered during two-stage procedures showed disappearance of the epithelial component, which prevented accurate diagnosis of malignancy. The enucleated tissue was completely excluded from blood flow, so inflammatory cell infiltration was typically absent and only the glandular duct structures were preserved. These pathological changes may be due to urinary infiltration as well as blood flow interruption, but the relationship was unclear without characteristic findings other than necrosis on pathology. This pathological change softened the enucleated tissue and improved the recovery efficiency. However, BBs remained in 33% of cases on Day 7, suggesting that softening is unlikely to occur in these tissue.

The morcellation efficiency on Day 7 was comparable to the 10.8 g/min reported by Ritter et al. [17] in their experiment, which aimed to identify the maximum efficiency of VersaCut using raw bovine heart as a phantom. These results suggested that we achieved the maximum recovery efficiency for the device.

Based on our results, an upper limit of enucleation in HoLEP does not exist and hypothermia associated with prolonged surgery is the major limitation to one-stage surgery. In particular, when using the reciprocating type, the risk of hypothermia is increased when the operating time exceeds 4 h for >200 g enucleated adenomas, due to the decrease in morcellation efficiency of about 1 g/min and need for BB treatment.

Because hypothermia occurred in our first two cases, we used a preplanned two-stage surgery for cases in whom the operation time was expected to exceed 4 h. We also decided to perform the two-stage surgery on Day 7, when recovery efficiency is maximal. Since these hospitalizations were funded by public insurance in Japan, the patients remained hospitalized between the surgeries. However, no major problems occurred during this period except for one case of Clavian—Dindo Grade II postoperative infection, which should be managed on an outpatient basis to reduce medical costs. In addition, the discomfort caused by the huge adenoma and catheter cuff in the bladder needs to be controlled.

Since pathological diagnosis is not possible in two-stage surgical cases, preoperative imaging tests and biopsy are necessary [18]. An oscillator-type morcellator can be expected to have a recovery efficiency of more than 3 g/min, even for adenomas weighing >300 g; therefore, surgery can be performed within 4 h even for adenomas weighing almost 500 g. HoLEP using an oscillating morcellator is the *de facto* size-independent surgical method. However, the oscillator-type morcellators, Piranha (Richard Wolf, Knittlingen, Germany) and DrillCut (Karl Storz, Tuttlingen, Germany), had 2.07% and 7.86% device failure incidence rates, respectively [4]; therefore, the informed consent for two-stage surgery or open conversion should be obtained prior to surgery.

High bladder incision for prolonged surgery is an option, but this is a relative indication, allowing the choice of two-stage surgery, unlike absolute indications such as hemorrhage or perforation. To determine the limits of pure endoscopic surgery, knowledge of morcellation efficiency in extreme conditions and temperature changes during surgery may be necessary. We believe that this study will provide useful information.

4.4. Limitations

The main limitation of our study was that it was conducted at a single institution and included a small number of cases. Therefore, it is necessary to accumulate more clinical data in future trials.

5. Conclusion

Two-stage morcellation using a reciprocating morcellator has shown efficiency that strongly correlates with the number of postoperative days, peaking on Day 7. This technique enables the safe endoscopic treatment of significant prostate enlargements reaching approximately 500 mL by skilled operators, demonstrating its effectiveness for substantial prostate volumes. Our findings indicate that two-stage morcellation is a viable option for managing larger cases of prostate enlargement, expanding the scope of endoscopic procedures.

Author contributions

Study concept, design and drafting of manuscript: Fumiyasu Endo.
Data acquisition: Kenji Komatsu.
Data analysis: Kazuhiro Ohwaki.
Critical revision of the manuscript: Masaki Shimbo, Kazunori Hattori.

Conflicts of interest

The authors declare no conflict of interest.

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