Research article

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Evaluation of early outcomes of extended lymphadenectomy in open radical cystectomy for bladder cancer

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Abstract

Objective: Evaluation of early outcomes of extended lymphadenectomy in open radical cystectomy for bladder cancer.

Methods: A descriptive case series study was conducted on 45 cases of extended lymphadenectomy from February 2023 to April 2024 at Binh Dan Hospital. Postoperative and 6-month follow-up outcomes were recorded, focusing on perioperative complications and early results.

Results: The average number of lymph nodes dissected was 13.7 ± 5.7 per case. Lymph node metastasis mapping showed that the further from the bladder, the lower the rate of lymph node metastasis. Tumors located in the left wall had the lowest rate of lymph node metastasis at 18.2%, corresponding to the lowest rate of left common iliac lymph node metastasis at 18.2%. A linear relationship was observed between the stage of bladder cancer and lymph node groups: the stage of nodal metastasis increased with the advancement of the primary tumor stage. The mean duration of lymph node dissection was 51.3 ± 11.2 minutes, accounting for 19.1% of the total surgical time. The mean duration of drainage was 8.9 ± 3.6 days, while the mean postoperative hospital stay was 9.9 ± 2.5 days. The average blood loss during lymph node dissection was 40.4 ± 27.8 ml, representing 8.9% of the total surgical blood loss. There were no perioperative complications during extended lymphadenectomy. Four cases (8.9%) of lymphocele were noted at 1 month postoperatively, of which one case required percutaneous drainage, and three cases resolved spontaneously after two weeks of follow-up (Clavien I 6.7% and Clavien IIIa 2.2%).

Conclusion: Extended lymphadenectomy in open radical cystectomy for bladder cancer is safe and feasible, contributing to accurate postoperative staging for subsequent treatment planning.

Keywords: extended lymphadenectomy (eLND), bladder cancer, radical cystectomy.

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1. INTRODUCTION

Bladder cancer is one of the most common malignancies in the urinary tract. According to GLOBOCAN statistics, bladder cancer ranked ninth in 2022, with 613,791 new cases and 220,349 deaths worldwide[1]. The treatment of bladder cancer has been standardized in urological association guidelines, with radical cystectomy being the standard treatment for muscle-invasive bladder cancer.

Pelvic lymphadenectomy during radical cystectomy is essential for staging, prognosis, and, in some cases, achieving

curative treatment in patients with regional lymph node metastases. Numerous studies have demonstrated that 20–25% of patients undergoing radical cystectomy have lymph node metastases at the time of surgery, making accurate identification of metastatic nodes crucial for initiating adjuvant chemotherapy with Cisplatin[2].

To date, urological guidelines remain inconsistent regarding the extent of lymphadenectomy[3]. Historically, lymph node dissection has included obturator, external iliac, and internal iliac lymph nodes, with the assumption that if these three groups were negative, the common iliac lymph nodes would also be uninvolved. However, some reports suggest that bladder cancer may metastasize early to higher anatomical sites, including the inferior mesenteric artery region. Herr et al. demonstrated that the greater the number of lymph nodes removed, the better the prognosis, with at least 10 lymph nodes removed during radical cystectomy improving 5-year survival rates from 44% to 61%[4]. Consequently, extended pelvic lymphadenectomy (eLND) has an important role in the treatment of bladder cancer.

A study on standard lymphadenectomy by Nguyen Ngoc Tien et al.[5] (2004) showed that tumor progression and poor differentiation were associated with increased lymph node metastasis. Meanwhile, a study on eLND in bladder cancer by Nguyen Van An et al.[6] (2012) reported cases of metastases in distant lymph node groups, while closer lymph node stations remained negative. This finding suggests that standard lymphadenectomy may be inadequate for accurate staging in some cases. Some studies on eLND have been conducted; however, there is still limited information available for reference in clinical practice. Consensus from various studies has defined eLND for bladder cancer as including the following lymph node groups: obturator and hypogastric, external iliac, common iliac, and presacral lymph nodes.

Thus, eLND may provide significant benefits in bladder cancer treatment, improving staging accuracy and guiding postoperative adjuvant therapy for better prognosis. However, our review of the literature suggests that limited research has been conducted on eLND, and debate regarding its benefits remains. Therefore, this study aims to address the question: "What are the early outcomes of eLND in open radical cystectomy for bladder cancer?"

2. METHODS

This study is a descriptive case series involving all patients diagnosed with bladder cancer and indicated for open radical cystectomy with eLND from February 2023 to October 2024 at Binh Dan Hospital, Ho Chi Minh City.

Patient Selection Criteria

Inclusion Criteria

Patients diagnosed with bladder cancer and treated at Binh Dan Hospital who meet the following conditions:

Indicated for open radical cystectomy.

Eligible for extended lymphadenectomy following open radical cystectomy.

Cancer staging: cT1 (high-risk), cT2 – T4a, cN1 – N3, cM0.

Patients with moderate to good general condition, assessed as ASA 1 – 3.

Exclusion Criteria

Patients with a history of prior pelvic surgery and/or radiation therapy for colorectal, uterine, or cervical cancer.

Patients previously treated with bladder-sparing multimodal therapy for

muscle-invasive bladder cancer, including complete transurethral resection of the tumor, partial cystectomy, radiotherapy, and chemotherapy.

Patients with diseases affecting the lymphatic system, including non-Hodgkin's lymphoma, Hodgkin's lymphoma, lymph node tuberculosis, lymphedema, lymphadenitis, and lymphangitis.

Preoperative Data Collection

Abdominal ultrasound and contrast-enhanced multislice computed tomography (MSCT) of the abdomen and pelvis were performed to assess bladder cancer staging, tumor invasion, and metastasis, as well as to evaluate radiological evidence of lymph node metastases.

Data from diagnostic cystoscopy, transurethral resection of bladder tumor, or bladder biopsy were reviewed to assess tumor morphology (papillary vs. cis), number, location, bladder neck involvement, and urethral invasion.

Surgical Procedure

Radical Cystectomy: A midline abdominal incision was made from hypogastric to the umbilicus, dissecting through the fascia and peritoneum. The median umbilical ligament was divided, and a retractor was placed for optimal exposure. Assessment of tumor invasion into surrounding tissues and presence of liver or peritoneal metastases were evaluated. The pelvic peritoneum was incised, and the ureters were dissected and divided. In female patients: The bladder, uterus, and anterior vaginal wall were removed en bloc. In male patients: The bladder, prostate, and seminal vesicles were resected en bloc.

Bilateral eLND was performed to evaluate lymph node metastases. Superior limit: Bifurcation of the abdominal aorta. Lateral limit: Genitofemoral nerve. Inferior limit: Highest deep inguinal node (Cloquet's node). Posterior limit: Hypogastric vessels, obturator fossa, and presacral region. Lymph Node Dissection by Anatomical Regions. Lymph nodes were dissected systematically in seven anatomical regions, with each group sent separately for histopathological examination[6,7].

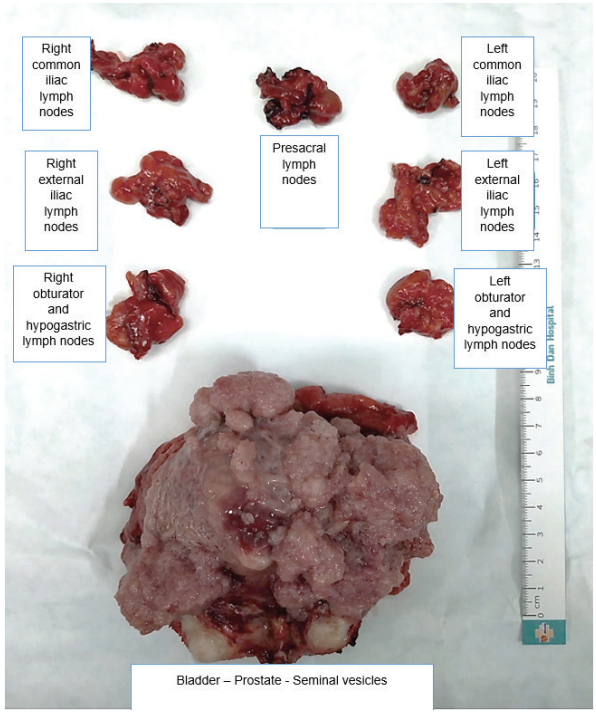

Figure 1. Bladder and the Seven Dissected Lymph Node Groups

Left obturator and hypogastric lymph nodes: Left common iliac artery bifurcation, pelvic floor, left external iliac artery, left pelvic wall, left internal iliac vessels, and left bladder wall.

Right obturator and hypogastric lymph nodes: Right common iliac artery bifurcation, pelvic floor, right external iliac artery, right pelvic wall, right internal iliac vessels, and right bladder wall.

Left external iliac lymph nodes: Left common iliac artery bifurcation, pelvic floor, left genitofemoral nerve, and left external iliac artery.

Right external iliac lymph nodes: Right common iliac artery bifurcation, pelvic

floor, right genitofemoral nerve, and right external iliac artery.

Left common iliac lymph nodes: Aortic bifurcation, left common iliac artery bifurcation, left genitofemoral nerve, and presacral lymph nodes.

Right common iliac lymph nodes: Aortic bifurcation, right common iliac artery bifurcation, right genitofemoral nerve, and presacral lymph nodes.

Presacral lymph nodes: Aortic bifurcation, bilateral common iliac arteries, and sacrum.

The bladder, prostate, seminal vesicles, and seven lymph node groups were fixed in formalin 10% in eight separate containers for histopathological evaluation. The bladder-prostate-seminal vesicle specimen was opened to ensure formalin penetration before submission to the pathology department for processing[8].

Following lymphadenectomy, urinary diversion or orthotopic neobladder reconstruction was performed based on individual patient factors. Pelvic drains were placed, and in cases of neobladder reconstruction, extraperitonealization of the neobladder was performed (or the peritoneum was used to cover the urinary diversion conduits). The abdominal wall was closed in layers, and all catheters and drainage tubes were secured properly.

Postoperative Monitoring

Monitoring of urinary drainage: Ureteral stents, suprapubic catheter, and urethral catheter were monitored based on the type of urinary diversion or neobladder reconstruction.

Drain output monitoring: Pelvic drain output was monitored, with drains typically removed on postoperative day 4–5, once fluid output ceased and ultrasound confirmed the absence of fluid collection.

The duration of postoperative hospitalization was recorded for all patients.

Lymph Node Specimen Processing

Macroscopic Examination: Number of lymph nodes in each dissected group; Size of the largest lymph node in each group; Morphology and coloration of the lymph nodes, along with suspected metastatic involvement.

Histopathological Processing: All lymph nodes were submitted for histopathological examination; Small lymph nodes (<3 mm) were submitted as a single specimen; Multiple small lymph nodes were embedded together in a single paraffin block; Larger lymph nodes were bisected or sectioned into 2–3 mm slices, maximizing the cross-sectional area, with each piece placed in separate paraffin blocks; Remaining tissue specimens were preserved in formalin, segregated by anatomical lymph node group; Hematoxylin and Eosin staining was performed for microscopic analysis.

Microscopic Evaluation: Specimens were examined under a light microscope, using objective lenses in sequence: Low magnification (4x and 10x) for general evaluation; High magnification (40x) for detailed cellular assessment; Photomicrographs were taken at 10x or 40x magnification, as needed.

Follow-Up at 1 Month Postoperatively

Abdominal ultrasound was performed to detect postoperative complications such as fluid collections, lymphatic leakage, or lymphoceles.

Systemic chemotherapy was administered if indicated, based on tumor staging and discussion with oncology specialists.

Follow-up at 1 month postoperatively continued, and we extended monitoring up to 6 months to identify other complications. Some cases were followed up for up to 20 months.

3. RESULTS

During the study period from February 2023 to October 2024 at Binh Dan Hospital, Ho Chi Minh City, we recorded 45 cases of eLND performed during open radical cystectomy for bladder cancer.

The mean duration of lymphadenectomy was 51.3 ± 11.2 minutes, accounting for 19.1% of the total surgical time. The most common duration was 50–60 minutes, observed in 22 cases (48.9%). The longest duration, >60 minutes, was noted in 6 cases (13.3%).

The mean blood loss during lymphadenectomy was 40.4 ± 27.8 ml, accounting for 8.9% of the total surgical blood loss. The highest blood loss recorded was 120 ml, occurring in a patient where 25 lymph nodes were dissected, 20 of which were metastatic.

The shortest duration was 5 days, while the longest was 21 days (mean: 8.9 ± 3.6 days). The longest drain duration (21 days) was observed in a case of neobladder-urethral anastomotic leakage. The shortest was 5 days, and the longest was 17 days (mean: 9.9 ± 2.5 days). The longest stay (17 days) was recorded in a patient with postoperative partial bowel obstruction.

Table 1. Postoperative Complications

Complication	Hospital Stay	1 Month	6–20 Months
Lymphocele	0	4	0
Surgical site infection	3	0	0
Ureter-enteric anastomotic leakage	1	0	0
Neobladder-urethral anastomotic leakage	1	0	0
Partial bowel obstruction	2	0	1
Urinary tract infection	0	0	11
Total	15.6%	8.9%	26.7%

Overall complication rates at different time points: Hospital stay: 15.6%, 1 month postoperatively: 8.9%, 6–20 months postoperatively: 26.7%; The most common complication during hospital stay was surgical site infection, occurring in 3 cases (6.7%); At 1 month postoperatively, the most frequent complication was lymphocele, observed in 4 cases (8.9%). One case required percutaneous drainage, while three cases resolved spontaneously within 2 weeks; At 6–20 months postoperatively, the most common complication was urinary tract infection, occurring in 11 cases (24.4%). These complications were recorded, and the patients were hospitalized for treatment.

The mean number of lymph nodes dissected per case was 13.7 ± 5.7, ranging from 5 to 30 nodes. The mean lymph node size was 1.8 ± 0.6 cm, with a minimum of 1 cm and a maximum of 4 cm. Among the 45 patients who underwent eLND, 11 cases (24.4%) were found to have lymph node metastases (N+).

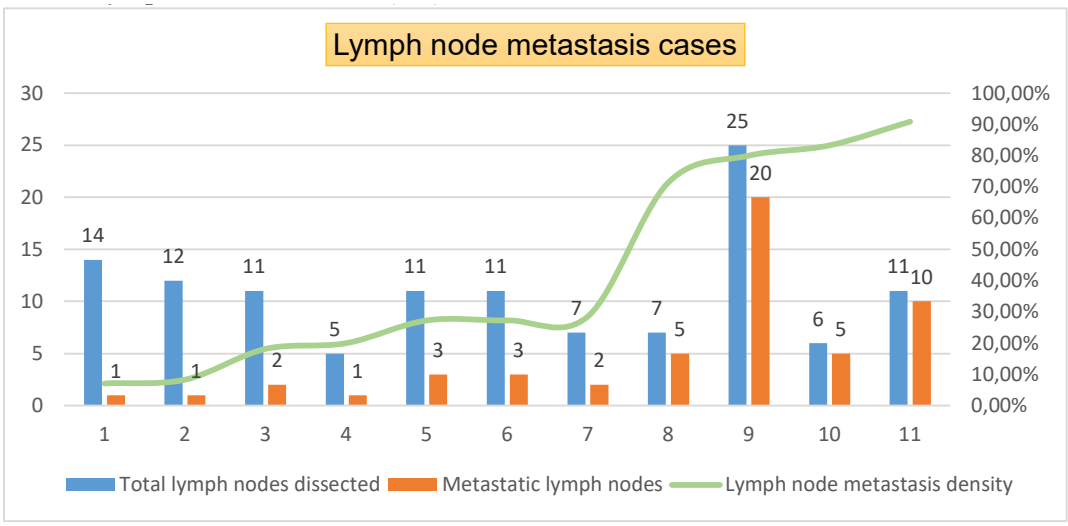

Figure 2. Distribution of Lymph Node Metastases

The chart illustrates the variation in the density of metastatic lymph nodes, ranging from 7.1% to 90.9%. Notably, some cases exhibited a very high metastatic lymph node density (>70%).

4.DISCUSSION

Lymphadenectomy Duration and Blood Loss

The mean duration of lymphadenectomy was 51.3 ± 11.2 minutes, accounting for 19.1% of the total surgical time. The surgical procedure consisted of three main phases: radical cystectomy, eLND, urinary diversion or orthotopic neobladder reconstruction. With lymphadenectomy comprising approximately 1:5 of the total operative time, our findings suggest that eLND does not significantly prolong the overall surgical duration.

The mean blood loss during lymphadenectomy accounted for 8.9% of the total intraoperative blood loss, with no cases requiring blood transfusion. Furthermore, blood loss was not associated with the urinary diversion technique. Our study, consistent with other research, indicates that lymphadenectomy does not substantially impact surgical prognosis.[6]

Complications Related to Lymphadenectomy

No major complications, such as large vessel injury, nerve damage, or gastrointestinal tract injury, were observed in this series. In some cases, minor bleeding from small tributaries of the inferior vena cava, common iliac vein, or external iliac vein was encountered but was successfully controlled intraoperatively.

Postoperative Drainage and Hospital Stay

To prevent lymphatic leakage and lymphocele formation, we placed bilateral pelvic drains in all patients. Drains were removed sequentially, based on ultrasound confirmation of fluid resolution or daily drainage output <50 ml.

Two cases required extended drainage beyond 14 days. Methylene Blue oral dye testing confirmed one case of uretero-enteric anastomotic leakage and one case of neobladder-urethral anastomotic leakage.

The longest postoperative hospital stay was 17 days in a patient with partial bowel obstruction, which was successfully managed conservatively.

Postoperative Complications Related to Lymphadenectomy

Postoperative complications specifically related to lymphadenectomy were observed in 4 cases (8.9%) of lymphocele, diagnosed by abdominal ultrasound at the 1-month follow-up: Three cases (3–4 cm lymphocele) were managed conservatively and resolved spontaneously within two weeks. One case (2.2%) had a large lymphocele (~10 cm), causing discomfort in the hypogastric region with ambulation, requiring percutaneous drainage under ultrasound guidance. This complication was classified as Clavien–Dindo grade IIIa.

Table 2. Comparison of Lymphocele Drainage Rates After eLND

Study	Number of Cases	Lymphadenectomy Technique	Lymphocele Requiring Drainage
Nguyễn Văn Ân[6]	9	eLND	0%
Lê Lương Vinh[9]	38	eLND	0%
Jürgen E Gschwend[10]	198	eLND	8.6%
Our Study	45	eLND	2.2%

Compared with other studies on eLND, we observed that as the number of surgical cases increases, the incidence of lymphocele formation also tends to rise. Additionally, the rate of lymphocele requiring intervention may increase proportionally.

Outcomes of Extended Pelvic Lymphadenectomy

Among the 11 cases with lymph node metastases (N+), we categorized metastatic rates across seven lymph node groups and generated a lymph node metastasis mapping diagram. Our findings indicate that metastatic lymph nodes were more prevalent in groups closer to the bladder and gradually decreased in distant nodal stations. This observation highlights a distinct difference between extended lymphadenectomy and standard/limited lymphadenectomy, as the common iliac and presacral lymph nodes are often omitted in standard dissections. Such an omission may lead to incomplete pathologic nodal (pN) staging, where a true pN3 stage may be misclassified as pN2 or pN1, potentially affecting postoperative prognosis and the decision for adjuvant chemotherapy.

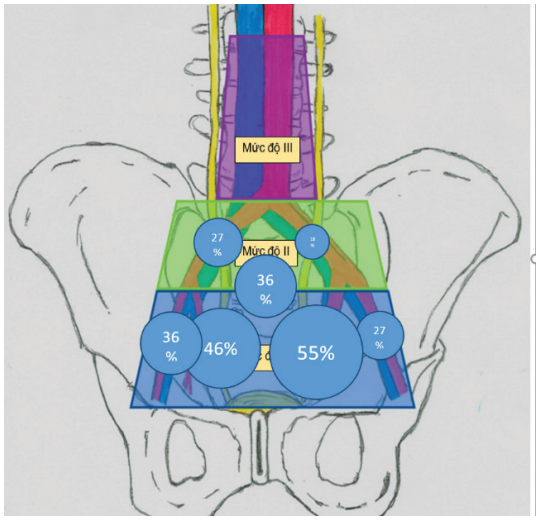

Figure 3. Lymph Node Metastasis Mapping

Thanks to the eLND technique, as well as the submission and analysis of each lymph node group separately (seven lymph node groups), we were able to stratify the extent of lymph node metastasis and map the metastatic lymphatic spread more accurately, in contrast to studies on standard lymphadenectomy.

We classified tumor locations within the bladder as follows: Left bladder wall tumors: 2/11 cases (18.2%), Right bladder wall tumors: 5/11 cases (45.5%), Bilateral or whole bladder tumors: 4/11 cases (36.4%). Our findings indicate that tumors located in the left bladder wall had the lowest incidence of lymph node metastases (18.2%), corresponding to the lowest rate of left common iliac lymph node metastases (18.2%). This suggests a tendency for lymphatic metastases to occur ipsilaterally to the primary tumor. Consequently, during lymphadenectomy, greater attention may be given to the side corresponding to the primary tumor.

With 36.4% of cases exhibiting metastases in the presacral lymph nodes, which are considered proximal lymphatic stations in bladder cancer metastasis, we recommend systematic dissection of this lymph node group in patients undergoing radical cystectomy, as it requires minimal additional surgical time.

In TNM staging, common iliac lymph nodes are classified as distant lymphatic stations (N3). The presence of just one metastatic lymph node in this region upstages the nodal classification to N3, leading to a minimum AJCC 8th edition stage of IIIB. This highlights the critical prognostic significance of these lymph nodes. Among 11 patients with lymph node metastases (N+), 4 cases (36.4%) had common iliac lymph node involvement (N3). If only standard lymphadenectomy had been performed, these 4 cases would have been missed, leading to incomplete nodal staging (N1/N2 instead of N3).

Table 3. Comparison of Common Iliac Lymph Node Metastases Rates

Study	Total Cases with N+	Cases with Common Iliac LN Metastases	Rate
Nguyễn Văn Ân[6]	5	1	20.0%
Lê Lương Vinh[9]	8	3	37.5%
Jose A. Pedrosa[11]	93	36	38.7%
Our Study	11	4	36.4%

Studies on eLND consistently report that one-third of cases with lymph node metastases involve the common iliac lymph nodes.[11] This high prevalence underscores the importance of routinely dissecting this lymph node group. During open surgery, dissection of tissue around the common iliac vessels is feasible, as the surgical field provides clear visualization. Therefore, incorporating common iliac lymphadenectomy in standard radical cystectomy protocols may enhance staging accuracy and guide postoperative management more effectively.

Correlation Between Tumor Stage (T) and Nodal Stage (N)

When stratifying lymph node metastasis (N+) rates according to tumor stage (T stage), we observed a progressive increase in lymph node involvement as tumor stage advanced. The lowest rate of nodal metastasis (6.3%) was found in pT1 cases,

whereas the highest rate (62.5%) was recorded in pT4 cases. To further analyze this trend, we compared the lymph node metastasis rates across different tumor stages between: The study by Nguyen Ngoc Tien et al.[5] (standard lymphadenectomy) and Our study (eLND)

Table 4. Comparison of Lymph Node Metastasis Rates by Tumor Stage

Tumor Stage (pT)	Nguyễn Ngọc Tiến[5] (n=68)			Our Study (n=45)		
	Patients	N+ Cases	Rate	Patients	N+ Cases	Rate
pT1	2	0	0.0%	16	1	6.3%
pT2a	18	2	11.0%	4	1	16.7%
pT2b	32	12	37.5%	4	2	50.0%
pT3	15	12	80.0%	9	2	22.2%
pT4	1	1	100.0%	8	5	62.5%

Both studies demonstrated an increasing trend of lymph node metastases with higher tumor stages (T stage). At pT4, the lymph node metastasis rate was 100% in the study by Nguyen Ngoc Tien et al. and 62.5% in our study.

The variability in metastasis rates between studies may be influenced by differences in lymphadenectomy techniques and the extent of node dissection. Further Spearman's rho correlation analysis between primary tumor stage (T) and lymph node metastasis stage (N) revealed: Correlation coefficient (ρ) = 0.439, p-value = 0.003 (statistically significant). This suggests that as the primary tumor invades deeper into and beyond the bladder, the likelihood of advanced lymph node metastases increases, aligning with existing oncological theories and previous research.

5. CONCLUSION

Extended pelvic lymphadenectomy during open radical cystectomy for bladder cancer is safe and feasible. It plays a crucial role in accurate postoperative staging, which is essential for determining subsequent treatment strategies.

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