Comparison of chondrosarcoma cases (grade I, II, III) current situations with clinical and statistical analysis among institutions.

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Abstract

Background Chondrosarcomas is a rare tumour that has a variable biological characteristic. Also, their treatment clinically and surgically is controversial. We performed a comparison review of different regional institutions series with the aim of assessing the clinical outcome of patients.

Purposes We, therefore, compare different institutions from different regions patients with grade 1 to 3 chondrosarcomas to (1) determine difference in survival rate, (2) local recurrence results, (3) determine successful outcome after surgery, (4) differences among surgical procedures. (5) Determine any association of clinical and demographic behaviour with gender, follow-up, treatment and chondrosarcoma affected body locations.

Methods A retrospective review of 33 chondrosarcoma(all grades) patient’s data since 2013, compared with 15 author’s total 868 patients research literature to find more about clinical and statistical advantages and similarities with our study. Here is mentioning of clinical information’s, surgery type categorised, adjuvants types, genders, follow-up years, recurrence, affected areas, death rates, successful outcome and survival rates by using statistical methods.

Results The overall survival rate was 94%, successful outcome 85% in 4.3 + 1.2 years follow-up. Observed wide resection, distilled water as adjuvant, chemo & radiotherapy significantly shows excellent result over our compared chondrosarcoma literature datas. We have also marked that females and humerus bone are more affected by chondrosarcoma among those literatures data.

Conclusions Low-grade chondrosarcoma of the skeleton can be treated with wide resection and by the use of distilled water, which give good oncological outcome and a
very low rate of post-surgical complications, as well as chondrosarcoma all grades recurrence.

**Background**

Chondrosarcoma is the 2nd most common malignant tumor of the skeleton.

Chondrosarcoma is a rare cancer with an estimated incidence of 1 in 200,000 per year \(^1\). The tumors have considerable variation in outcome depending on size, histologic grade, Musculoskeletal Tumor Society (MSTS) stage \(^2\), and tumor type. All kinds of tumors have different characteristics and biological differences. Chondrosarcoma grade and the anatomical site are important because of both influences the sort of treatment and result. The chondrosarcoma can affect any part of the bone but has a predilection for pelvis, femur, and proximal humerus \(^3\). Surgery procedures do not always recommend treatment; neither chemotherapy nor radiation therapy is effective in this tumor \(^4\). For this tumor male prevalence of two: one, and this usually occurs in the third and fifth decade of a lifetime \(^5, 6\). This tumor of the pelvis is the most aggressive and has the lowest survival rate \(^7, 8\). Chondrosarcomas are malignant cartilaginous neoplasms with distinct morphological features and clinical behavior. Among all primary malignant tumors of the skeleton, this rare tumor is 20% \(^9\). People still making wrong decisions because of a lack of awareness about the treatment of their tumor. So that the survival rate is low and the health care system couldn’t help big numbers of people who do not come to hospitals for treatment, but they waste time with quacks or bonesetters. It happens because of many social and cultural factors that patient continues to visit such peoples \(^10\). The motive of this research is to the comparison among regions chondrosarcoma patient’s cases. The goal of this article is not to discuss our accuracy or outcome of
chondrosarcoma grades, notwithstanding to look for the weight of the information come up with their clinical information & history, surgical, survival rate, infections, complications, functional and gender for better analytical understanding.

2. **Surgical & treatment information**

Surgical treatments are mainly recommended for most types of chondrosarcoma, and probably surgery used for a newly diagnosed tumor or if recurrence occurs. Particular treatment for chondrosarcoma will be definite healthcare provider based on overall health, medical history, Type, stage (extent), cancer location, age, tolerance for specific medicines, procedures, different therapies, course of the disease and its expected result, patient’s opinions, and preferences. Enormous of authors suggested wide resections for grade two and three tumors for extra compartmental Grade 1 lesion \(^4; 11; 12\). Few authors recommend wide resection, while others are convinced by intralesional resection augmented with a surgical adjuvant, such as LN\(_2\), C\(_6\)H\(_5\)OH (phenol), electrocautery and argon-beam laser, is adequate \(^13; 14\). Unfortunately, biopsy in the chondral intramedullary lesion is not reliable \(^15; 16\). Tumor grading often misleads the surgeon to inapplicable surgery. Clinical history and imaging studies are significant when choosing the appropriate surgical technic. We have done 17 wide angel resection, seven marginal resections, two intralesional resections. We collected the age, gender, follow-up (months), anatomical locations, staging according to the Enneking system\(^{17}\). Follow as a usual pre-operative surgical procedure in our hospital according to the patient’s present situation and body conditions. During surgeries, the patient’s position for the spine was the prone and supine position for extremity. The target for the treatment is to remove the mass and reduce the possibility that it will cause recurrence. The following kinds of surgeries may
be used:-

Resection, Curettage, Bone cement, Limb-sparing surgery, Amputation, Reconstructive surgery, Biopsy. Several authors agree to use this technique for tumor cells [18]. The tumor cells will be inactive in due course sop in distilled water for 60 s at 55°C, and the tumor cell death rate was 100%. Tumor cells can be destroyed by distilled water for 60 s at 55°C, which is proved in several author’s literatures. This way of treatment provides a new fast and low cost tumor-free technic to inactivate tumor cells, as well as attached to surgical instruments[18]. However, in some cases of chondrosarcoma tumor, intralesional excision may not be adequate, for example, because of an intra-articular or pelvic localization or large size[19]. In some cases, a greater tendency to metastasize or progress occurs with axial-pelvic tumors, which also has higher local recurrence rates [20]. There are 14 fracture cases; we believe that the fractures occur more because of lack of osteosynthesis, although there is no enough data to prove it. The distinction between wide resection and marginal resection was based on a combination of the pathology report and the operative note. Each of These techniques carries different risks and benefits. Also, by the developing of medical science, everyday new methods and techniques are used by doctors, which outcome is slightly better and efficient. In our hospital, we have followed all pre-surgical procedures according to Chinese medical ethics, rules, and regulations.

**Figure 1**

**Figure 2**

**2.1. Post-operative follow-up**

Patients come for evaluation is first two years every 3 months once, the next five years every 6 months once and annually once after that. Radiographs and physical exam were performed at each time. If local recurrence was suspected, then additional imaging was
requested, such as a CT scan or MRI. Chemotherapy and radiotherapy were used for a few malignant tumor patients. If there is lung metastasis, then determine with CT. Tumor margins were evaluated accordingly. Cost of the potential immediate post-surgical neurologic deficits against the advantage of long-term survival should factor heavily into the treatment strategy, also taken part decision making with the patients.

2.2. Radio & Chemo therapy

If chondrosarcoma tumor can't be removed with surgical procedures, then external beam radiotherapy may be used to treat it. This therapy may apply to destroy any cancer cells after wide resection which left behind. Radiotherapy is also used if the tumor is a recurrence. Based on the skull or in the spinal bones tumor treat by apply of conformal proton beam radiation therapy or intensity-modulated radiation therapy. For low grade chondrosarcoma usually chemotherapy not use due to showing no improve survival rate. Another minimal invasive percutaneous technique is radiofrequency ablation, which is used mainly for palliating painful bone metastasis [21; 22]. But we haven’t done any study or addressing the application of this technique in tumors and more specifically, chondrosarcoma tumors.

Methods

We conducted a formal review of any published literature from the last 20 years related to chondrosarcoma types and grades in internet-based journals and PubMed. Were performed to optimize capture all relevant studies. The strength of evidence was then graded for each chondrosarcoma measure. Level of evidence for our studies collects from 15 author's institution research papers with total 868 patients for comparison with our patient's data, such as –systemic review of homogenous level 1, prospective cohort study, systemic analysis, case-control studies or series, expert opinions. Patient's data about pre-
operative and post-operative tumor grading was collected from the files of our hospital database, which was completed. Patients treated in the author’s institution for all grade chondrosarcoma of bones from 2013 to 2019 was performed as a retrospective review. Few patients were kept out from the current study because of the follow-up was less than 24 months or lack of clinical data. The inclusion data were based on extracted directory from the full database records. This study was approved by the General Hospital of Ningxia Medical University committee for clinical research; also informed consent was gathered from the patients participating.

Results

We have found that using distilled water as an adjuvant during tumor surgeries has an excellent effect. Only 6.1% of our patient's tumor recurrence but didn’t switch their chondrosarcoma grades from one to another. Distilled water shows better outcome (survived 31 patients) over phenol, liquid nitrogen or H$_2$O$_2$ as an adjuvant in all of our patient's surgeries, which is one of the most significant founding in our study than other authors.

Also, we have seen that wide resection may help chondrosarcoma patients achieve high survival rate in 5 to 10 years follow-up with 85% successful outcome.

Other regions, according to the author’s literature (table 2&3), we have found that female patients are affected more by chondrosarcoma than our area, which is different than previous chondrosarcoma literature studies.

Pre and post-operative surgery, our patients take chemotherapy and radiotherapy, which is slightly different than other regions treatments; it may help achieve a highly successful outcome with avoiding minimum death rate.

Statistical data comparison total 901 patients (table 2 &3) shows that most patients affected by chondrosarcoma on limbs area of their body among all of the literature.

There is 0% distant metastasis among our patients.

5. **Statistical information and analysis**

SPSS v24.0 was used to perform the statistical analyses for the patient's data. Here we have compared our hospital all grades chondrosarcoma patient’s data with 13 author’s chondrosarcoma research literature from different regions in table 2, and two authors in table 3, total 15 author’s research literature and total 868 patients were included for comparison. Time and age intervals were regarded as continuous variables. Table 1 we
are going to analyses our collected data from our hospital database. All tests here were two sided, and a p-value <0.05 was considered significant. This series of the patient’s treated from 2013 and recorded in the hospital database. We found that 33 patients had grade 1 to 3 types of chondrosarcoma. In this article, patients age range 16 to 79 years(46.7±16.7) and their follow-up years 4.3±1.2. Our patient’s male-female ratio is 23:10, where 69.7% of patients are male. As we know, chondrosarcoma affects male more than female. In 13 patients were tumors located in the humerus 13(39.39%), 9(27.27%) femur, 5(15.15%) tibia, 4(12.12%) pelvis, 2(6.06%) scapula and other areas such as spine is 9(27.27%). Out of 33 patients, 31 patients did surgery, and two patients went to the oncology department to getting chemotherapy cycle first. Patients Tumor size is 6.3±3.7 cm. Our patients were staying hospital according to their chondrosarcoma grade (1-3), pre and post-surgical situations 17±12.8 days. 19(57.56%) patients had other major diseases such as lung infections, bone tuberculosis, sciatica, herniation, degeneration, and few of them had a past surgical history as well. 14 patients had fracture in different locations, which is 42.4% among all 33 patients. 23 patients had metastasis, which is 69.69%, and 10 patients are the benign stage of chondrosarcoma tumor. So we can say most of the patients had I & II grade chondrosarcoma tumor. Our experts have done biopsy all of our patients. There is 1 patient who had an amputation, to avoid recurrence and spread in other parts of the body. 2 patients died after surgery within 2 years follow-up. 8(24.2%) patients had a bone graft, and 13 (39.39%) patients had metallic implants because of fractures occurred due to lack of bone density. We also used bone cement in 5(16%) cases out of 31. There are 13(39%) patients surgeries were curettage. We have chosen wide resection for most patients, which is about 17(54.83%) cases, marginal resection was 7(21.21%), and intralesional resection was 2. We sent to our oncology department 2 patients for complete 3 cycle chemotherapy and suggested to do surgery after that. Total
9 (27%) patients had chemotherapy and radiotherapy before or after surgery. Total death with the disease during follow-up years is 2 (6.1%), which is considerable. Because of those two patients had grade 3 chondrosarcoma. Our hospital total successful outcome is 28(84.84%), because of their motion, the function was up to the mark (including metallic implants), and no chondrosarcoma recurrence occurred among them. The total survival rate, according to our follow-up years, is 31(93.90%) patients.

**Table 2 & 3** recorded a total of 15 authors and their literature included factors are below: author’s name, gender, type of tumor, locations and diagnosis of tumor, years (months) follow-up, age, surgical procedures, types of adjuvants, defects after done curettage, recurrence, metastasis, fractures in post-operative, switching grade (from one grade to another grade), death, bone graft, tumor characteristics, survival rate, outcome, chemo & radiotherapy, metallic implants, other diseases in these two tables mentioned. Was done the comparison with our hospital data among their literature information’s, because of getting more accurate comparison results to know more about current outcomes of chondrosarcoma.

**Discussion**

We recognize the diagnosis and treatment of these tumors have evolved with time, and some treatment of these lesions treated long ago might be treated differently today. The same primary tumor treated with an amputation during the early period of our study may be treated with wide excision today. Each of these techniques carries different risks and benefits. Although most of the chondrosarcoma grades (1, 2 & 3) and subtypes, surgical treatment offering only chances for recovery from the disease, it’s still debated about the most optimal surgical management. If we consider morbidity and a demanding reconstruction, depending on the location followed by local adjuvant treatment, for example, liquid nitrogen/distilled water, and bone graft with wide resection can lead to
promising long-term clinical outcomes. But using distilled water as an adjuvant during our all surgical procedures shows the better outcome, because of only 2(6.1%) recurrence cases we have seen among all chondrosarcoma grade patients. Most of these cases, the preferred choice for our surgical treatment was remaining wide resection. As compared with all of the author’s literature, chondrosarcoma grade is 1 or low grade, although 20(61%) patients from our data are grade 2. Other regions author’s literature (table 2& 3) most of their patients are affected on limbs as same as our patients, which shows no differences. Total follow-up years of other author’s literature are slightly longer than us, but it’s not changed these rare tumor cases result much. There are no defects noticed after curettage among our patients, but few patients, among other author’s literature (table 2& 3), shows there are defects. There is very low (6.1%) recurrence after surgery among our patients, but most of the other author’s (table 2& 3) data shows that their patient's tumor recurrences are 1/3rd. Most of the author’s mentioned that they use adjuvants, such as phenol, liquid nitrogen or cryoprobes or H2O2 for surgery, but we are using distilled water only for protect recurrence, and the result is adequate with reasonable survival rate 94%. Few author’s(table 2& 3) data shows there are post-operative fractures; on the other hand, there is no available data about in our study. Few authors (table 2& 3) literature data shows in the table that fewer is switch to a different grade of chondrosarcoma, wherein our data there is none. Table 3, we have low rate amputation, but the higher rate in mourikis a et al. chondrosarcoma affect mostly male than female but mourikis a et al. (n=31), and bindiganavile et al. (n=125) literature shows female is more than male. Our institution death rate with the disease is lower than bindiganavile et al. than a Korean institution. Bindiganavile et al. data show low metastasis than mourikis a et al. and our data. Metallic implant, fracture, and a bone graft
is the high rate in mourikis a et al. data than our, in other hands, there is no data about it in bindiganavile et al. literature. Our institution, 27.27% of patients had taken chemo & radiotherapy, which is a very high rate than other author’s patient's data. We have got 42% of patients who has another major disease, but there is no data available among other author’s literature. Total survival and successful outcome among our patients is 94% and 85%, which is better than the UK and Korean institutions (table 3).

This study has a few limits. 1st, it is not a prospective study, but the rarity of this tumor and the need for extended clinical follow-up make it challenging. 2nd, comparison of different treatments was not randomized, but based on current information about this pathology; 3rd, the monitoring of our patients is significant, but still too short for considerations with outcomes.

Conclusions

After optimal diagnosis and treat by an experienced team of specialists, although chondrosarcoma tumors generally have an excellent prognosis. Analysis of the difference between surgical technics and patient outcomes has been limited due to the sparseness of these lesions and few institutions having enough patients and data. Also, different regions and institutions surgical, clinical diagnosis, and treatment are slightly not similar. We observed that females are get affected more than male among those institutions chondrosarcoma patients, which is alarming somehow, because of chondrosarcoma characteristic may changing gradually around the globe. Although our study found that using distilled water as an adjuvant and wide resection giving significantly better results for grade 1 & 2 chondrosarcoma treatment among our 33 patients than compared institutions patients, the total survival rate is 91% and a successful outcome is 85%. To
get more accuracy and evidence of this result need to conduct further research in clinical basis because of relatively short follow-up and non-randomized study limitations. This is a systematic review which is a relatively high level of generalizability due to the inclusion of patients among institutions and countries. It may also be susceptible to bias associated with individual patients being reported over others.

Declarations

8.1 Authors’ contribution

All authors approved the final manuscript.

8.2. Ethics approval to participate

Review board approval was obtained before starting research.

8.3 Consent for publication

Not applicable.

8.4 Availability of data and material

On reasonable request data portion will be available, but all data are not publicly available, because of patient’s information.

8.5 Competing interests

All authors have no competing interests.

8.6. Funding Information

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8.7. Acknowledgments

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8.8. Abbreviations

Not applicable

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**Tables**

**Table 1:** Chinese hospital patient’s clinical data statistical information:

| Variables                              | Total n (%) | Successful outcome n (%) | Non-successful outcome n (%) |
|----------------------------------------|-------------|--------------------------|------------------------------|
| Age, (mean±SD)                         | 46.7±16.7   | 43.2±15.1                | 59.9(16.8)                   |
| Follow year, (mean±SD)                | 4.3±1.2     | 4.2±1.1                  | 4.5±1.7                      |
| Gender                                 |             |                          |                              |
| Male                                   | 23(69.7)    | 16(61.5)                 | 7(100.0)                     |
| Female                                 | 10(30.3)    | 10(38.5)                 | 0(0)                         |
| Tumor size(cm), (mean±SD)             | 6.3±3.7     | 6.0±3.9                  | 7.4±2.7                      |
| Stay in hospital, (mean±SD)           | 17.5±12.8   | 18.9±13.1                | 12.3±10.8                    |
| Fracture, yes                          | 14(42.4)    | 11(42.3)                 | 3(42.9)                      |
| Biopsy and Resection, yes             | 31(93.9)    | 0(0)                     | 5(71.4)                      |
| Amputation, yes                        | 1(3.0)      | 0(0)                     | 1(14.3)                      |
| Death with disease, yes                | 2(6.1)      | 0(0)                     | 2(28.6)                      |
| Metastasis and malignant, yes          | 26(78.8)    | 19(73.1)                 | 7(100.0)                     |
| Allograft, yes                         | 8(24.2)     | 7(26.9)                  | 1(14.3)                      |
| Benign, yes                            | 10(30.3)    | 10(38.5)                 | 7(100.0)                     |
| No surgery, yes                        | 2(6.1)      | 0(0)                     | 2(28.6)                      |
| Other major Disease, yes              | 19(57.6)    | 14(53.8)                 | 5(71.4)                      |
| Metallic implant                       | 13(39)      |                          |                              |
| Chemotherapy & radiotherapy            | 9(27)       |                          |                              |
| Total patient                          |             | 28(84.84)                |                              |
| Total patient survive                  |             | 31(93.93)                |                              |
#: Fisher exact test. A p-value less than <.05 are not significant

Table 2 Treatment and results for low-grade chondrosarcoma in recent literature:

| Author [Ref.]     | No. of patients, sites | Diagnosis        | Follow-up (months) | Surgical treatment (no. of patients) | Adjuvants (other than cement) | Filling of the defect after curettage | Recurrence (%) |
|-------------------|------------------------|------------------|--------------------|--------------------------------------|--------------------------------|---------------------------------------|----------------|
| Verdegaal et al.[23] | 85 limbs               | CS low gr        | 86                 | curettage                            | Phenol                        | Allograft                             | 5.9            |
| Funovics et al.[24] | 70 limbs               | CS low gr        | 81                 | Resection-36, curettage-34           | None                          | Cement                                |                |
| Andreou et al.[25]  | 56 low gr/total 115 all grade & site | CS gr 1         | 144                | Curettage or Resection                | NA                            | NA                                    | 26.8           |
| Donate et al.[26]   | 31 limbs               | CS gr 1          | 157                | Resection-16, curettage-15           | Phenol-9, liquid nitr-3, none-3 | Cement-6, allograft-1, cement-2, none-4 |                |
| Mohler et al.[27]   | 46 limbs               | CS gr 1/enchondroma | 47                 | curettage                            | Liquid nitr+H₂O₂               | Resection-10, cement-7, other-5        | 4.3            |
| Souna et al.[28]    | 15 limbs               | CS gr 1          | 96                 | curettage                            | Liquid nitrogen                | None                                   | 0              |
| Aarons et al.[29]   | 32 limbs               | CS gr 1          | 55                 | Resection-15, curettage-17           | Phenol-6, liquid nitr-3, H₂O₂-1, none-7 | Resection-16, curettage-15          |                |
| Hanna et al.[30]    | 39 limbs               | CS gr 1/CS gr 0.5| 61                 | curettage                            | None                          | Cement                                | 5              |
| Van der Geest et al.[31] | 130 NA               | CS gr 1/enchondroma | 60                 | curettage                            | Liquid nitrogen                | Allograft, cement-3                    | 1.5            |
| Streitburger et al.[14] | 69 all sites            | CS gr 1         | 78.5               | Resection-60, wide marg.-40, curettage-9 | H₂O₂                           | Cement                                | 14.5           |
| Leerapun et al.[32] | 70 limbs               | CS gr 1          | 102                | Resection-57, curettage-13           | phenol                        | Bone graft-12, cement-1               | 2.8            |
| Ahlmann et al.[33]  | 10 all sites           | CS low gr        | 38.5               | curettage                            | Argon gas cryoprobes          | None                                   | 0              |
| **Our series**      | **33 all sites**       | **CS gr 1-3**    | **51.6**           | **Wide -17, marg.-7, Distilled water** | **None**                      | **None (31 patients had surgery)**    | **6.1**        |

*gr* grade, *NA* not available data, *Intrales-* intralesional margins, *Margin* marginal margins, *CS* chondrosarcoma.
Table 3 - chondrosarcoma patients data compare with UK & Korean institution.

| Name                          | China- our hospital | UK- Mourikis A et al[^34] | Korea |
|-------------------------------|---------------------|---------------------------|-------|
| Total patient                 | 33                  | 31                        | 125   |
| Age (mean±sd)                 | 46.7±16.7           | 42±17                     | 14.77 |
| Follow-up year(mean±sd)       | 4.3±1.2             | 16±8                      | 9.1±5 |
| Male : female                 | 23:10               | 13:18                     | 59:66 |
| Tumor size                    | 6.3±3.7 cm(mean±sd) | NA                        | < 100 |
| Amputation                    | 1(3%)               | 21(6774%)                 | NA    |
| Death with disease            | 2(6.1%)             | 2(6.45%)                  | 17    |
| Metastasis                    | 23(69.7%)           | 25(80.64%)                | 9     |
| Bone graft/allograft          | Bone graft 8(24%)   | 31 all patients           | NA    |
| Total successful outcome      | 28 (85%)            | 24(77%)                   | 100(81)|
| Total survival                | 31(94%)             | 29(93.54%)                | 106(84)|
| Metallic implants             | 13(39%)             | 26(83.87%)                | NA    |
| Fractures                     | 14(42.4%)           | 28(90.32%)                | NA    |
| CS-grade 1,2,3                | 10,20,3             | Grade1 /low grade         | 62,21, |
| wide resection                | 17(54.83%)          | 7                         | 40(52%)|
| Marginal resection            | 7                   | 3                         | 5     |
| Intralesional resection       | 2                   | 1                         | 48(43%)|
| Chemotherapy &radiotherapy    | 9(27.27%)           | 1                         | NA    |
| With another major disease    | 14(42.42%)          | NA                        | NA    |
| Humerus                       | 13(39.39%)          | 31                        | Proxir|
| Femur                         | 9(27.27%)           | 76(from 499 total patients)| 30(34%)|
| Tibia                         | 5(15.15%)           | 20                        | 20(22%)|
| Pelvis                        | 4(12.12%)           | 23                        | Proxir|
| Other body part affected by CS| 11 ((33.33%)        | NA                        | 6 (4.8%)|

NA= no data available

Figures
Figure 1

Postoperative imaging data a: Immediately after surgery, the X-ray film showed good ulnar and radial end-to-end alignment; b: CT+3D reconstruction showed bone graft reconstruction healing after 3 months; c: X-ray film showed reconstruction bone 3 months after operation and no recurrence, d: 9 months after operation, the reconstructed bone end healed; e: 2 years after surgery, the reconstructed bone end was completely fused, no elbow joint, wrist dislocation, no tumor relapse
Figure 2
Flowchart of chondrosarcoma surgical management.

Supplementary Files
This is a list of supplementary files associated with the primary manuscript. Click to download.
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