

Characteristics Of Mass Size: Differentiating Leiomyosarcoma, Atypical Leiomyoma, and Typical Leiomyoma in Magnetic Resonance Imaging

Linda M. Tompodung^{a*}, Tri Wulanhandarini^a, Lies Mardiyana^a, Widiana Ferriastuti^a

* linda_tompodung@rocketmail.com

^a Department of Radiology, Faculty of Medicine, Airlangga University/Universitas Soetomo Hospital, Surabaya, East Java, Indonesia

Abstract

Background and Purpose: Leiomyoma and leiomyosarcoma of uteri have similar clinical symptoms and overlapping imaging presentations but different prognoses. Preoperative diagnostics are essential. We aim to investigate whether mass size in Magnetic resonance (MR) features can differentiate leiomyosarcoma (LMS) from atypical leiomyoma (ALM) and Typical Leiomyoma (LM).

Methods: This retrospective study included 43 female patients with pathologically confirmed (LMS=2, ALM=23, LM=18) imaged with MRI before surgery. We evaluated the tumor volume with one-way ANOVA and post hoc Dunn's multiple comparisons.

Results: Typical leiomyoma was associated with a smaller size (diameter 5,4 cm; volume 170 cm³) and was significantly different from atypical leiomyoma (diameter 14,3 cm; volume 1.032 cm³) (P < 0.001). However, atypical leiomyoma is large and cannot be differentiated from leiomyosarcoma (diameter 13,1 cm; volume 951 cm³).

Conclusions: Mass size can be valuable for differentiating leiomyoma typical from atypical but not leiomyosarcoma from typical and atypical leiomyoma. Multiparametric analysis is required to determine atypical leiomyoma and leiomyosarcoma.

Keywords: Leiomyoma, atypical leiomyoma, leiomyosarcoma, tumor size

1. Introduction

Uterine leiomyoma is a benign mass of myometrial smooth muscle cells and is the most common uterine mass. In contrast, uterine leiomyosarcoma is a malignant mass that represents 1% of uterine corpus malignancies with a poor prognosis. Clinically, leiomyoma and leiomyosarcoma are challenging to differentiate because they have the same clinical symptoms, but their treatment is very different [1,2,3]. Treatment of leiomyosarcoma requires surgical procedures such as hysterectomy and salpingo-oophorectomy [4]. Leiomyomas can be treated without surgery, including medical drug therapy, high-intensity focused ultrasound (HIFU) therapy, uterine artery embolization or minimally invasive surgery, and fibroid enucleation where uterine function is still preserved [4,5].

The size of the mass is one indicator in determining whether a tumor is benign or malignant [1,6]. It is able to calculate the tumor size, number, and boundaries on MRI. The size of the mass (diameter) is said to be an

indication in determining prognostics. Previous research by Nordal et al. (1995) showed that FIGO stage and tumor size were factors in deciding prognostics [7]. Therefore, this study aimed to evaluate mass size from MRI in differentiating leiomyosarcoma from leiomyoma atypical and leiomyoma typical preoperative.

2. Material and Method

A Retrospective study has been performed on 43 female patients (LMS=2, ALM=23, LM=18) who underwent MR examination with a diagnosis of typical, atypical leiomyoma, and leiomyosarcoma, all of which were diagnosed by uterine tumor biopsy in the years 2021 until 2023. All tissues were used with the approval of the Ethics Committee after written informed consent had been obtained from the patients.

The measure of mass is the amount of mass calculated in diameters and volume. Calculations based on diameter are calculated by measuring the diameter of the largest mass in each orthogonal measurement plane (Antero-posterior, Medial-lateral and Cranio-Caudal) then multiplying by 0.52. ellipsoid formula ($V = dcc \times dl \times dap \times 0.52$) to calculate diameter based on volume (V). where dcc is the craniocaudal diameter, dap is the anteroposterior diameter and dl is the lateral diameter (Figure 1) [8].

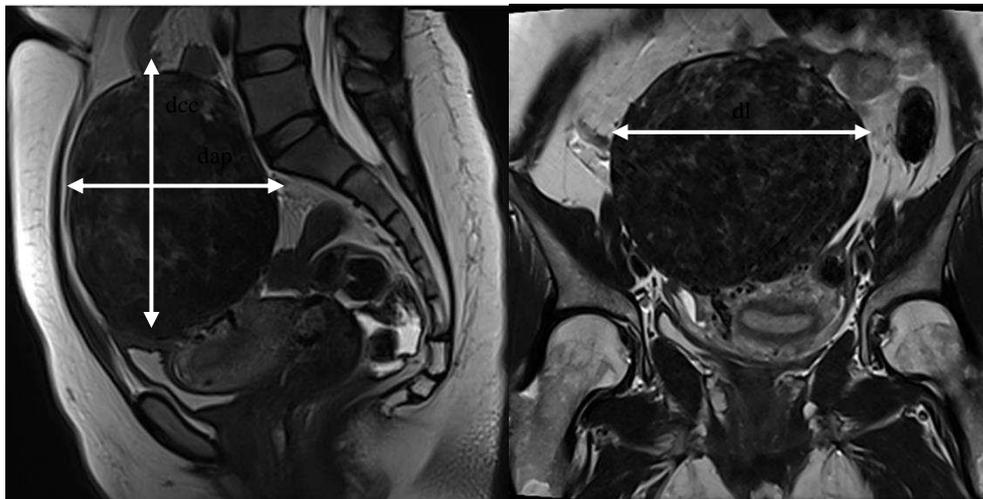


Figure 1. Ellipsoid formula ($V = dcc \times dl \times dap \times 0.52$) to calculate volume-based diameter (V). where dcc is the craniocaudal diameter, dap is the anteroposterior diameter and dl is the lateral diameter.

All statistical analyses were performed using software packages version (SPSS) with a consider statically significant level of $\alpha = < 0.05$. Associations between mass size on MRI and histopathologic diagnosis with differences in distributions of leiomyosarcoma were assessed by one-way ANOVA with post hoc Dunn's multiple comparisons.

3. Results and Discussion

The distribution of average mean, minimum, and maximum volumes and diameters of typical leiomyomas, atypical leiomyomas, and leiomyosarcomas are shown in Table 1, 2 and Figure 2. The average volume of leiomyoma was 170 cm³ with a standard deviation of 237, followed by leiomyosarcoma, 951 cm³ with a standard deviation of 854, and the average volume of atypical leiomyoma 951 cm³ with a standard deviation of 984. The smallest volume obtained was 0.17 cm³, and the largest was 3.989 cm³. We performed a one-way ANOVA with post hoc Dunn's multiple comparisons to compare the tumor volume between these three groups. A significant volume difference between typical LM and ALM was observed ($p < 0,0001$), while there is no difference between typical LM versus LMS and ALM versus LMS.

Table 1. Diameter for each tumor category (cm)

| Tumor | Mean Diameter (Median) | Minimum Diameter | Maximum Diameter |
|---------------------------|---------------------------|------------------|------------------|
| Leiomyosarcoma (n = 2) | 13,1 ± 6,9 (13,1) | 8,2 | 18,0 |
| Leiomyoma Atypical (n=23) | 14,3 ± 4,5 (14,8) | 8,0 | 20,2 |
| Leiomyoma typical (n=18) | 5,4 ± 14,3 (4) | 1,4 | 12,6 |

Table 2. Volume for each tumor category (cm³)

| Tumor | Mean Volume (Median) | Minimum Volume | Maximum Volume |
|---------------------------|-------------------------|----------------|----------------|
| Leiomyosarcoma (n = 2) | 951 ± 984 (952) | 252 | 1.651 |
| Leiomyoma Atypical (n=23) | 1.032 ± 854 (862) | 200 | 3.989 |
| Leiomyoma typical (n=18) | 170 ± 237 (35) | 0,17 | 713 |

The size of the leiomyoma and leiomyosarcoma mass was calculated (largest size) Antero posteriorly, mediolaterally, and cranio-caudally then multiplied by 0.52 to obtain the mass volume. In molecular biology, research by Rein et al (1998) concluded that there was a significant relationship between cytogenetic abnormalities and leiomyoma size, this shows that the chromosomal abnormalities associated with each leiomyoma influence mass growth [9]. In this study the average size of typical leiomyomas was 170 cm³ SD ± 237, atypical leiomyomas 1,032 cm³. SD ± 854 and leiomyosarcoma 951 cm³ SD ± 984. The smallest volume obtained was 0.17 cm³ and the largest was 3.989 cm³. Guoruj et al (2020) used a mass diameter ≥7 cm as a predictor for differentiating uterine leiomyoma and leiomyosarcoma [10]. From the research results, there were masses measuring >7 cm in typical leiomyomas and atypical leiomyomas. It was also found that the average mass diameter in typical leiomyomas was 5.4 ± 14.3 cm and atypical leiomyomas was 14.3 ± 4.5 cm, while leiomyosarcoma was 13.1 ± 6.9 cm.

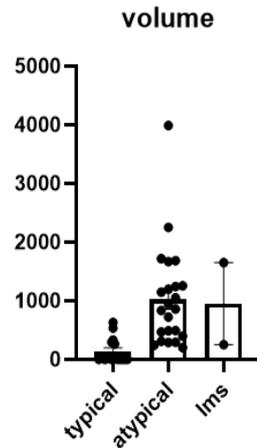


Figure 2. Mass volume distribution in typical leiomyoma, atypical leiomyoma, and leiomyosarcoma

Han's (2013) research on 276 leiomyoma sufferers found that the size of the degenerating leiomyoma was between 5.2 and 15.5 cm with an average of 7.7 cm [11]. In contrast, in this study, the size was between 8.0 – 20.2 cm, with an average of 14.3 ± 4.5 cm in atypical leiomyoma. Research by Rio et al. (2019) concluded that the mass size of atypical uterine leiomyoma and leiomyosarcoma was not statistically significant in differentiating between the two masses [12]. Thomassin-Naggara (2013) is in line with Rio's research, which stated that there was no difference in size between benign and malignant masses [13]. Our study finds that lesion size did not help distinguish between LMS from typical leiomyoma or atypical leiomyoma. Still, there was a significant difference in size between typical leiomyoma and atypical leiomyoma.

The volume or size of the mass in leiomyosarcoma is related to the prognosis. Size <5 cm has a 5-year survival rate of 64%, size 5 -10 cm 56.4%, and mass size > 10 cm 29.3% [14]. Lu et al. (2020) also obtained the same results with univariate and multivariate analysis; a mass size of less or more than 10 cm was associated with a 5-year survival rate [15]. In our study, we have 2 cases of LMS; one was < 10 cm and the other was > 10 cm in size. The Atypical leiomyoma (17 out of 23) were > 10 cm, and 2 cases were > 20 cm, but size >10 cm in typical leiomyoma is not much (2 out of 18).

4. Conclusion

Mass size can be valuable for differentiating leiomyoma typical from atypical but not leiomyosarcoma from typical and atypical leiomyoma. Multiparametric analysis is required to determine atypical leiomyoma and leiomyosarcoma. There are several limitations in this research. First, the sample distribution was uneven due to the rarity of leiomyosarcoma cases. Second, in volume measurements, we did not use automatic MRI volume entry but used calculations using the ellipsoid formula ($V = d_{cc} \times d_l \times d_{ap} \times 0.52$) so that it was less representative of the edges of the lobulated mass.

5. References.

1. Demulder, D; Ascher, SM. Uterine leiomyosarcoma: Can MRI differentiate leiomyosarcoma from benign leiomyoma before treatment?. *American Journal of Roentgenology*, 2018, 211.6: 1405-1415.
2. Sun, S., et al. How to differentiate uterine leiomyosarcoma from leiomyoma with imaging. *Diagnostic and interventional imaging*, 2019, 100.10: 619-634.
3. Žak, K, et al. Preoperative differentiation of uterine leiomyomas and leiomyosarcomas: current possibilities and future directions. *Cancers*, 2022, 14.8: 1966.
4. Gadducci, A, et al. The management of patients with uterine sarcoma: a debated clinical challenge. *Critical reviews in oncology/hematology*, 2008, 65.2: 129-142. George, S., Serrano,., Hensley, M. L., & Ray-Coquard, I. (2018). Soft tissue and uterine leiomyosarcoma. *Journal of Clinical Oncology*, 36(2), 144.
5. George, S, et al. Soft tissue and uterine leiomyosarcoma. *Journal of Clinical Oncology*, 2018, 36.2: 144.
6. Cho, H, et al. Differential diagnosis between uterine sarcoma and leiomyoma using preoperative clinical characteristics. *Journal of Obstetrics and Gynaecology Research*, 2016, 42.3: 313-318.
7. Nordal, R. R., Kristensen, G. B., Kern, J., Stenwig, A. E., Pettersen, E. O., & Tropé, C. G. (1995). The prognostic significance of 'stage, tumor size, cellular atypia and DNA ploidy in uterine leiomyosarcoma. *Acta Oncologica*, 34(6), 797-802.
8. Kim, H. J., & Kim, W. (2012). Method of tumor volume evaluation using magnetic resonance imaging for outcome prediction in cervical cancer treated with concurrent chemotherapy and radiotherapy. *Radiation oncology journal*, 30(2), 70.
9. Rein, MS., et al. Cytogenetic abnormalities in uterine myomas are associated with myoma size. *Molecular human reproduction*, 1998, 4.1: 83-86. Žak, K., Zaremba, B., Rajtak, A., Kotarski, J., Amant, F., & Bobiński, M. (2022). Preoperative differentiation of uterine leiomyomas and leiomyosarcomas: current possibilities and future directions. *Cancers*, 14(8), 1966.
10. Žak, K, et al. Preoperative differentiation of uterine leiomyomas and leiomyosarcomas: current possibilities and future directions. *Cancers*, 2022, 14.8: 1966.
11. Han, SC, et al. Degeneration of leiomyoma in patients referred for uterine fibroid embolization: incidence, imaging features and clinical characteristics. *Yonsei medical journal*, 2013, 54.1: 215-219.
12. Rio, Gisela, et al. T2 hyperintense myometrial tumors: can MRI features differentiate leiomyomas from leiomyosarcomas?. *Abdominal Radiology*, 2019, 44: 3388-3397.
13. Thomassin-Naggara, I, et al. How to differentiate benign from malignant myometrial tumours using MR imaging. *European radiology*, 2013, 23: 2306-2314.
14. Abeler, VM., et al. Uterine sarcomas in Norway. A histopathological and prognostic survey of a total population from 1970 to 2000 including 419 patients. *Histopathology*, 2009, 54.3: 355-364.
15. Lu, Y, et al. A nomogram for predicting overall survival in patients with uterine leiomyosarcoma: a SEER population-based study. *Future Oncology*, 2020, 16.10: 573-584.