

# Are there any Connections between Adrenal Myelolipoma and Hypertension?

**Lede Lin**

Sichuan University West China Hospital

**Lina Gong**

Sichuan University West China Hospital

**Wenjin Sun**

Sichuan University West China Hospital

**Liang Cheng**

Sichuan University West China Hospital

**Hong Li**

Sichuan University West China Hospital

**Kunjie Wang**

Sichuan University West China Hospital

**Yuchun Zhu** (✉ [mmaalleee@126.com](mailto:mmaalleee@126.com))

Department of Urology, Institute of Urology (Laboratory of Reconstructive Urology), West China Hospital, Sichuan University, Chengdu, Sichuan, P.R.C. <https://orcid.org/0000-0002-6140-2586>

---

## Research article

**Keywords:** Adrenal myelolipoma, hypertension, surgery, remission, connections

**Posted Date:** September 2nd, 2019

**DOI:** <https://doi.org/10.21203/rs.2.13870/v1>

**License:**   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

# Abstract

**Background.** Adrenal myelolipoma (AML) is a non-functional benign neoplasm from adrenal cortex, composed of mature fat and hematopoietic tissue. Usually, patients have no symptoms. However, some present with hypertension and blood pressure normalizes after surgery, indicating some connections between AML and hypertension. **Methods .** This is a retrospective cohort study of 372 patients diagnosed with AML from September 2008 to December 2018 collected in Urology Department of West China Hospital, Chengdu, Sichuan, China. We collected clinical records of patients before surgery and partial patients were done with hormone examination. Postoperative follow-up was also done for those with hypertension and whether patients needed to take antihypertensive drugs and postoperative blood pressure were recorded. We aim to explore the characteristics of both AML patients with hypertension and remission of hypertension in 1 year after surgery. **Results.** There were 372 AML patients included in the study, 159 males and 213 females, aged  $49.77\pm 11.64$  years old. Among them, 118 patients presented with hypertension. The percentage of hypertension in each subgroup increased with age. Sixty patients were followed up for 1 to 9 years, with a median follow-up of 52 months. The course of hypertension in the remission group was shorter than that in the non-remission group ( $P=0.020$ ), and tumor lateralization was significantly different between two groups ( $P=0.005$ ). **Conclusion.** Nearly one third of AML patients suffered from hypertension in our study and there do exist some potential links between AML and hypertension.

## Introduction

Adrenal myelolipoma(AML) is generally considered a non-functional benign tumor originated from adrenal cortex, made up of variable proportion of mature fat and hematopoietic tissues[1]. The number of case-reports about AML has considerably increased in recent years, which may be related to the development and wide application of imaging techniques, resulting in an increase in detection of adrenal incidentaloma including AML[2]. Female patients are more common and the predilection age is 50-70 years old, with right lesions more prevalent than those in the left [1,3]. Initially, the neoplasm is asymptomatic, which is discovered during routine physical examination accidentally. However, some are diagnosed with AML due to lumbar pain, abdominal pain, dizziness, abnormal level of hormones and so on[4,5]. Some patients present with hypertension and are eventually diagnosed as AML by histopathological biopsy. There has been several reports on the normalized blood pressure following surgery of AML resection, suggesting that there may be a relationship between hypertension and AML [6,7,8]. Hence, we aim to explore the characteristics of both AML patients with hypertension and remission of hypertension in 1 year after surgery.

## Methods

### Participants

This is a retrospective cohort study of 372 patients diagnosed with AML from September 2008 to December 2018 collected in Urology Department of West China Hospital, Chengdu, Sichuan, China. All patients were treated with surgery.

### **Including and excluding criteria**

The including criteria of this study were as follows: ☐neoplasm from adrenal cortex presented by computer tomography(Figure 1); ☐neoplasm more than 4 centimeters or complicated with hypertension or other symptoms☐patients who underwent surgical removal of adrenal neoplasm; ☐diagnosis of AML confirmed by pathological examination after surgery(Figure 2).

The excluding criteria of this study were as follows: ☐diagnosis of other tumor by symptoms, laboratory examination and postoperative pathological examination, such as pheochromocytoma, primary aldosteronism and other adrenal diseases that may cause hypertension; ☐AML patients combined with diseases detailed in ☐; ☐patients with adrenal neoplasm that did not undergo a surgery.

### **Data**

We collected clinical records of patients before surgery, consisting of gender, age, leading complaints (including lumbar pain and abdominal pain), history of diabetes, tumor lateralization, tumor diameter, body mass index (BMI), duration of hypertension, blood pressure and the number of antihypertensive drugs. Postoperative follow-up was also done for those with hypertension and whether patients needed to take antihypertensive drugs and postoperative blood pressure were recorded regularly at each follow-up.

### **Intervention**

All eligible patients were divided into two groups: hypertension and non-hypertension, based on the complication of hypertension( systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg measured 3 times on different two days, or having started antihypertensive therapy). Based on the outcomes of follow-up, those with hypertension were divided into two groups:the remission group and the non-remission group. The remission of hypertension after the operation is defined as stopping the use of antihypertensive drugs for 3 months and the blood pressure coming down to normal ( $< 140/90$ mmHg), which lasts till the end of follow-up.

### **Statistical analysis**

All the procedures were finished on the statistical software, IBM SPSS Statistics 22. Discrete variables were reported as percentage, and continuous variables as mean $\pm$  standard deviation (SD) or median (quartile). For analysis of categorical variables, Pearson  $\chi^2$  or Fisher Exact Test was used. Differences between means were tested with Student T test. Receiver operation characteristic (ROC) curve was utilized to examine the efficacy of a diagnostic model.  $P < 0.05$  was applied to certify the statistical significance between two groups of data. Normality of the distribution was tested using the Shapiro - Wilk test.

# Results

## Baseline characteristics

There were 372 eligible AML patients enrolled in our study, comprising of 159 males and 213 females. The average age was  $49.77 \pm 11.64$  years, among which 118 patients complicated with hypertension. The course of hypertension ranged from 1 days to 30 years and the mean systolic and diastolic pressure in hypertension group is  $168.89 \pm 23.18$  mmHg and  $99.29 \pm 14.82$  mmHg, respectively. Antihypertensive drugs included nifedipine, amlodipine, captopril, irbesartan, metoprolol, prazosin, furosemide and so on. The incidence of hypertension in AML is 31.7%.

## Characteristics of AML with hypertension

Data were analyzed in subgroup of age and the demographic and clinical features were detailed in Table 1 and Supplement Table 1. We found that the percentage of hypertension in each subgroup increased with age. The lateralization in hypertension group was significantly different from that in non-hypertension group. However, there was no significant difference in tumor lateralization and tumor diameter in each subgroup, except for subgroup of age 20-29 and age 70-79.

## Characteristics of hypertension remission in 1 year after surgery

Among 118 cases of AML complicated with hypertension, we finished following up 60 with follow-up time of 1-9 years. The median follow-up time was 52 months. There were 16 patients not using drugs in 1 year after operation, whose blood pressure returned to normal and continued till the end of the first year. Three patients stopped taking antihypertensive drugs after operation, nonetheless, the blood pressure rose again in three weeks, 1 year and 2 years after operation, respectively, and their blood pressure was controlled well by taking antihypertensive drugs. While 43 patients needed to continue to take antihypertensive drugs after operation, and the blood pressure was well controlled. The number of antihypertensive drugs and level of blood pressure are not significantly different before and after surgery.

There was significant difference in the lateralization of tumor between the remission group and the non-remission group, with P value < 0.05. (Table 2) As for the course of hypertension, we utilized Wilcoxon rank sum test to ensure the inspection efficacy, proving that the statistical difference was significant. The remission rate was 26.67% in 1 year after the surgical treatment, while 22.22% (10 out of 45 cases) in 3 years, and 7 cases of 28 cases were with normal blood pressure value in the 5-year follow-up after operation. Cases with normal blood pressure had no further potential increase in blood pressure requiring antihypertensive medication.

ROC curve (Figure 3) was used to test the efficacy of course of hypertension to distinguish remission group from non-remission group in Table 2 and we were able to see the area under curve (AUC) is significant, with P value = 0.020. Thirteen out of 14 cases in remission group were of hypertension course no more than 3 years and the other one with 10 years of hypertension. The information in Table 3 showed that the cutoff of course of hypertension as  $\leq 3$  years distinguished hypertension remission group from

non-remission group, with sensitivity of 92.9% and specificity of 58.7%. The positive predictive value was 40.6% and the negative predictive value was 96.4%.

## Discussion

In this study, we aim to explore characteristics of both AML patients with hypertension and remission of hypertension in 1 year after surgery. Based on our study, AML patients were usually diagnosed at the age of  $49.77 \pm 11.64$  on average, which is in consistence with the report of Decmann A[5] who reviewed 440 cases of AML with mean age of  $51 \pm 14.4$ . The incidence of AML with hypertension in our study is 31.7%, while 22.3% of AML with hypertension was reported by Decmann A[5]. It seems that there may exist some intrinsic connections between AML and hypertension.

On one hand, AML patients may be complicated with primary hypertension. In this study, we found that the proportion of hypertension in each subgroup in Supplement Table 1 increased with age, which is also a clinical risk characteristic of primary hypertension[9]. If AML patients are complicated with primary hypertension, implying their blood pressure is not directly related to AML, the possibility of hypertension relief after operation will be low.

On the other hand, we found an interesting phenomenon in our research that more AML were located on the right side, with a proportion of 63.7%. Several studies[1,10,11] also reported this phenomenon. The cause of this phenomenon may be attributed to the pathogenesis of AML. Here comes a theory that adipose tissue originating from mesenchymal stem cells harbors in adrenal cortex and causes inflammatory reaction under certain stimulation, which is the first step in forming AML.[12] In our human body, the right adrenal gland faces more possibility of friction from the inferior border of liver when we breath, which serves as a sort of stimuli contributing to the appearance of AML. However, the pathogenesis is even more complicated and perhaps involves with hormonal pathways. Further experimental data may reveal the the reason why there is a dominant right-sided AML.

In our study, we found that the important characteristics of hypertension remission in 1 year after surgery was the course of hypertension. The shorter the course of hypertension, the greater the possibility of blood pressure returning to normal after operation. After the lesion is surgically removed, compression effect on the kidney is relieved, and hypertension is alleviated. However, some patients' blood pressure did not return to normal, and we think, apart from primary hypertension, it may also be associated with the long duration of renal compression, leading to inflammation and promoting fibrosis, which causes irreversible damage to kidneys and blood vessels. Accordingly, blood pressure has not returned to a normal level after operation. However, we did not obtain all patients' hormone data in remission and non-remission group, before and after surgery. If the level of plasma renin activity goes down to normal after operation, our hypothesis will stand. In Table 3, we set a cutoff of  $\leq 3$  years to predict if AML with hypertension will relieve after operation. If a patient undergoes AML surgery, whose hypertension course is more than 3 years, his possibility of remission is relatively low, partially due to primary hypertension or

the long duration of renal compression. Adequate cases with hormone data are needed to prove our idea and our study may provide some theoretical evidences.

Table 2 also presents a thought-provoking outcome. In the remission group, almost all cases (13/14) were from the right side. We discovered that the mean diameter of right-sided tumor in remission group was larger than that of left-side tumor in remission group, but not significantly. Was this phenomenon attributed to a lack of samples or some reasons like anatomical difference between left and right adrenal gland in our human body? We still do not know and more clinical and experimental data are needed.

## Conclusions

Nearly one third of AML patients suffered from hypertension in our study and there do exist some potential links between AML and hypertension. To be more specific, AML patients with hypertension are more likely to result from getting old rather than endocrine function of AML itself and a AML patient with hypertension more than 3 years is less likely to get relieved. It is regretful this is a retrospective cohort study and there is a limit to the resources, so more further prospective studies are needed to explore and certify the results of our study.

## List Of Abbreviations

Adrenal myelolipoma (AML)

Body mass index (BMI)

Standard deviation (SD)

Receiver operation characteristic (ROC)

Area under curve (AUC)

## Declarations

### Ethics approval and consent to participate

The study is approved by the Ethics Committee of West China Hospital of Sichuan University. No informed consent for research is obtained from each individual because all the clinical records are acquired retrospectively from Hospital Inpatient System (HIS) when patients were admitted to hospital for diagnosis and treatment.

### Consent for publication

Not applicable.

### Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### Competing interests

The authors declare that they have no competing interests.

### Funding

The work is supported by the 1.3.5 project for disciplines of excellence, West China Hospital, Sichuan University (ZY2016104), the Innovation Spark Project of Sichuan University (2018SCUH0061), [the National Natural Science Fund of China \(81770703\)](#), [the National Natural Science Fund of China \(81470927\)](#) and [the National Natural Science Fund of China \(81800667\)](#).

### Authors' contributions

Conception and design of study: L L and L G; Acquisition of data (laboratory or clinical): L L, W S, and L Ch; Data analysis and/or interpretation: L L and L Ch; Drafting of manuscript and/or critical revision: L L, L G, H L, K W and Y Zh; Approval of final version of manuscript: H L, K W, and Y Zh.

### Acknowledgements

None.

## References

1. Lam AK. Lipomatous tumours in adrenal gland: WHO updates and clinical implications. *Endocrine-related cancer*, 2017, 24: R65-R79.
2. Yin L, Teng J, Zhou Q, et al. A 10-year single-center experience with surgical management of adrenal myelolipoma. *Journal of Endourology*, 2014, 28: 252-255.
3. Nabi J, Rafiq D, Authoy FN, Sofi GN. Incidental Detection of Adrenal Myelolipoma: A Case Report and Review of Literature. *Case Reports in Urology*, 2013, 2013:789481.
4. Liu HP, Chang WY, Chien ST, et al. Intra-abdominal bleeding with hemorrhagic shock: a case of adrenal myelolipoma and review of literature. *BMC surgery*, 2017, 17: 74.
5. Decmann A, Perge P, Toth M, Lgaz P. Adrenal myelolipoma: a comprehensive review. *Endocrine*, 2018, 59: 7-15.
6. Udupa S, Usha M, Visweswara RN, Desai MG. Left-sided giant adrenal myelolipoma secreting catecholamine. *Indian J Pathol Microbiol*, 2012, 55: 389-391.
7. Tamidari H, Mishra AK, Gupta S, Agarwal A. Catecholamine secreting adrenal myelolipoma. *Indian J Med Sci*. 2006, 60:331–333.
8. Jakka N, Venkateswarlu J, Satyavani N, Neelavani K, Ramesh J. Functioning adrenal myelolipoma: A rare cause of hypertension. *Indian Journal of Endocrinology & Metabolism*, 2013, 17: 249-251.

9. Chen WW, Gao RL, Liu LS, et al. China cardiovascular diseases report 2015: a summary. *J Geriatr Cardiol*, 2017, 14: 1-10.
10. Shenoy VG, Thota A, Shankar R, Desai MG. Adrenal myelolipoma: Controversies in its management. *Indian. J. Urol*, 2015,31: 94–101.
11. Lam AK. Update on adrenal tumours in 2017 World Health Organization (WHO) of Endocrine Tumours. *Endocr. Pathol*, 2017: 1–15.
12. Feng C, Jiang H, Ding Q, Wen H. Adrenal myelolipoma: A mingle of progenitor cells? *Med. Hypotheses*, 2013, 80, 819–822.

## Tables

**Table 1. Characteristics of AML patients with hypertension**

| <b>Demographic and clinical features</b>           | <b>Hypertension</b> | <b>Non-hypertension</b> | <b>P value</b> |
|--|---------------------|-------------------------|----------------|
| <b>Number of cases(%)</b>                          | 118(31.7%)          | 254(68.3%)              |                |
| <b>Mean age <math>\pm</math> SD, years</b>         | 54.97 $\pm$ 10.18   | 47.36 $\pm$ 11.50       | <0.001         |
| <b>Sex, males/females</b>                          | 53/65               | 106/148                 | 0.564          |
| <b>Leading complaints(%)</b>                       | 23(19.5%)           | 47(18.5%)               | 0.821          |
| <b>Diabetes mellitus(%)</b>                        | 16(13.6%)           | 19(7.5%)                | 0.062          |
| <b>Tumor location, left/right/bilateral</b>        | 52/66/0             | 78/171/5                | 0.009          |
| <b>Mean tumor diameter <math>\pm</math> SD, cm</b> | 6.10 $\pm$ 3.04     | 5.80 $\pm$ 2.86         | 0.352          |

AML: adrenal myelolipoma; SD:standard deviation

Leading complaints include lumbar pain and abdominal pain.

**Table 2. Characteristics of hypertension in 1 year after surgery**

| Demographic and clinical features            | Remission           | Non-remission           | P value |
|--|---------------------|-------------------------|---------|
| Number of cases(%)                           | 14#(23.3%)          | 46(76.7%)               |         |
| Mean age $\pm$ SD, years                     | 54.14 $\pm$ 10.01   | 54.89 $\pm$ 10.09       | 0.809   |
| Sex, males/females                           | 7/7                 | 17/29                   | 0.535   |
| Mean BMI $\pm$ SD, kg/m <sup>2</sup>         | 24.95 $\pm$ 2.32    | 25.86 $\pm$ 3.63        | 0.273   |
| Leading complaints(%)                        | 2(14.3%)            | 6(13.0%)                | 1.000   |
| Median course of hypertension(quartile), d   | 272.5<br>(52.5,730) | 1642.5<br>(225,3011.25) | 0.020   |
| Tumor location, left/right                   | 1/13                | 23/23                   | 0.005   |
| Mean left-sided tumor diameter $\pm$ SD, cm  | 3                   | 5.82 $\pm$ 2.11         | 0.204   |
| Mean right-sided tumor diameter $\pm$ SD, cm | 5.55 $\pm$ 2.51     | 6.23 $\pm$ 3.38         | 0.534   |

SD:standard deviation; BMI: body mass index

Leading complaints include lumbar pain and abdominal pain.

#:There were actually 16 cases in the remission group, however, the blood pressure in two of them rose again in 1 year and 2 years after operation, respectively. Therefore, we put those two cases in the non-remission group.

**Table 3. Evaluation of course of hypertension ( $\leq$ 3 years as a cutoff)**

|                     | Remission | Non-remission | Total number |
|---------------------|-----------|---------------|--------------|
| $\leq$ 3 years      | 13        | 19            | 32           |
| $>$ 3years          | 1         | 27            | 28           |
| <b>Total number</b> | <b>14</b> | <b>46</b>     | <b>60</b>    |

## Additional File

File name: Lede Lin Supplement Table 1

Title of data: Supplement Table 1. Characteristics of AML patients with hypertension

Description of data: Data were analyzed in subgroup of age and the demographic and clinical features were detailed in Supplement Table 1

## Figures

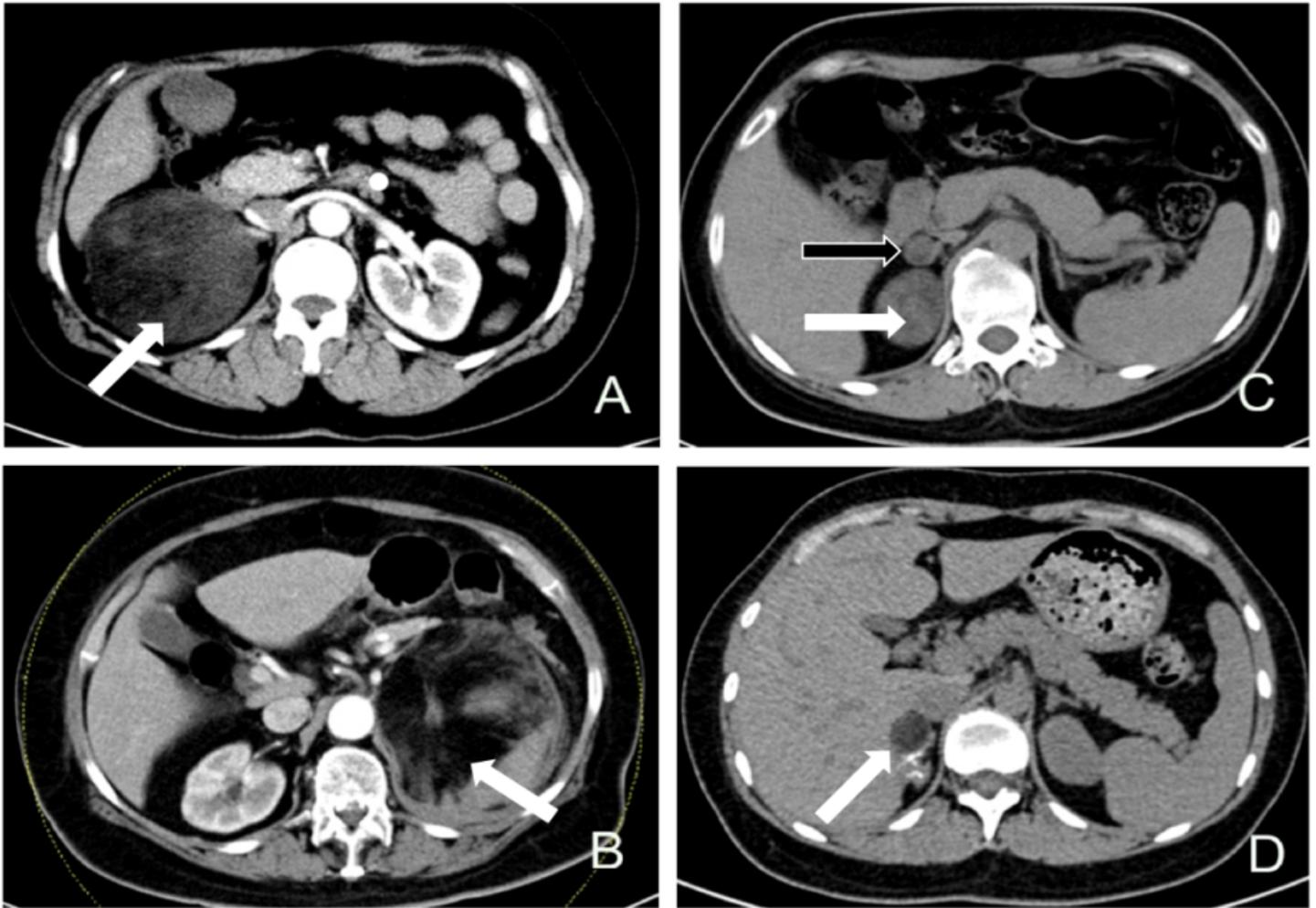
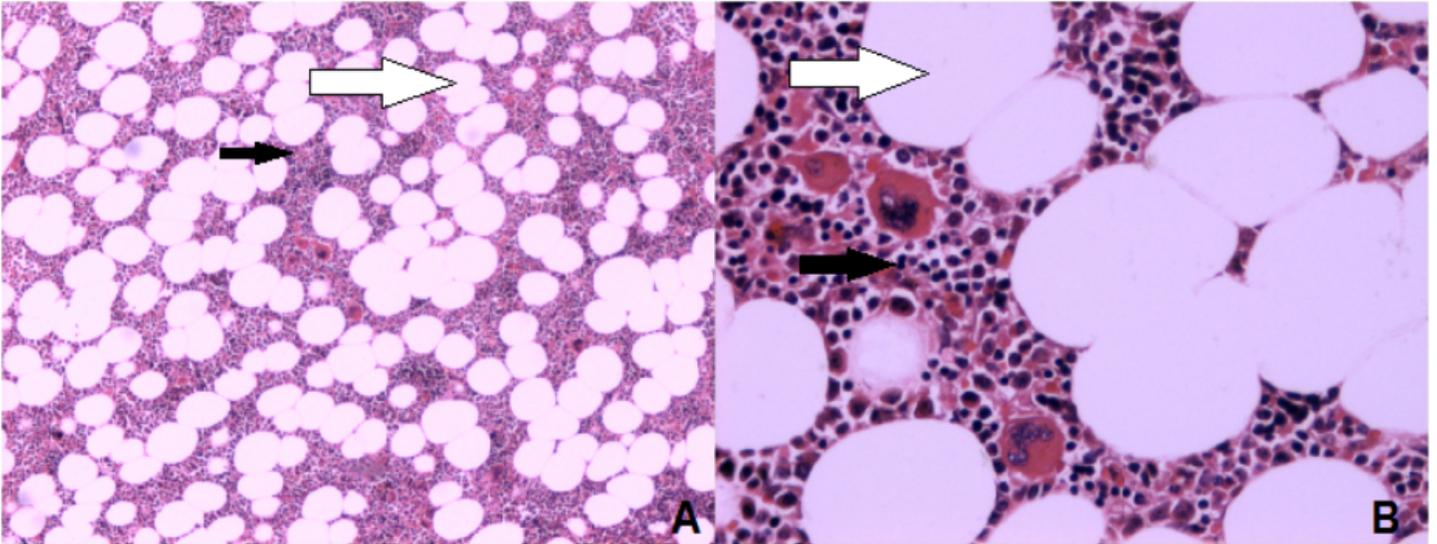


Figure 1

A. A huge adrenal neoplasm located in the right side (white arrow) B. A huge adrenal neoplasm located in the left side (white arrow) C. Multiple adrenal neoplasm located in the right side (white and black arrow) D. A recurrent adrenal neoplasm after surgical treatment of AML 2 years ago (white arrow)



**Figure 2**

AML is made up of mature fat tissue (white arrow) and hematopoietic tissues (black arrow) in pathological histological specimen. A. Hematoxylin-eosin staining of AML( $\times 50$ ) B. Hematoxylin-eosin staining of AML( $\times 200$ )

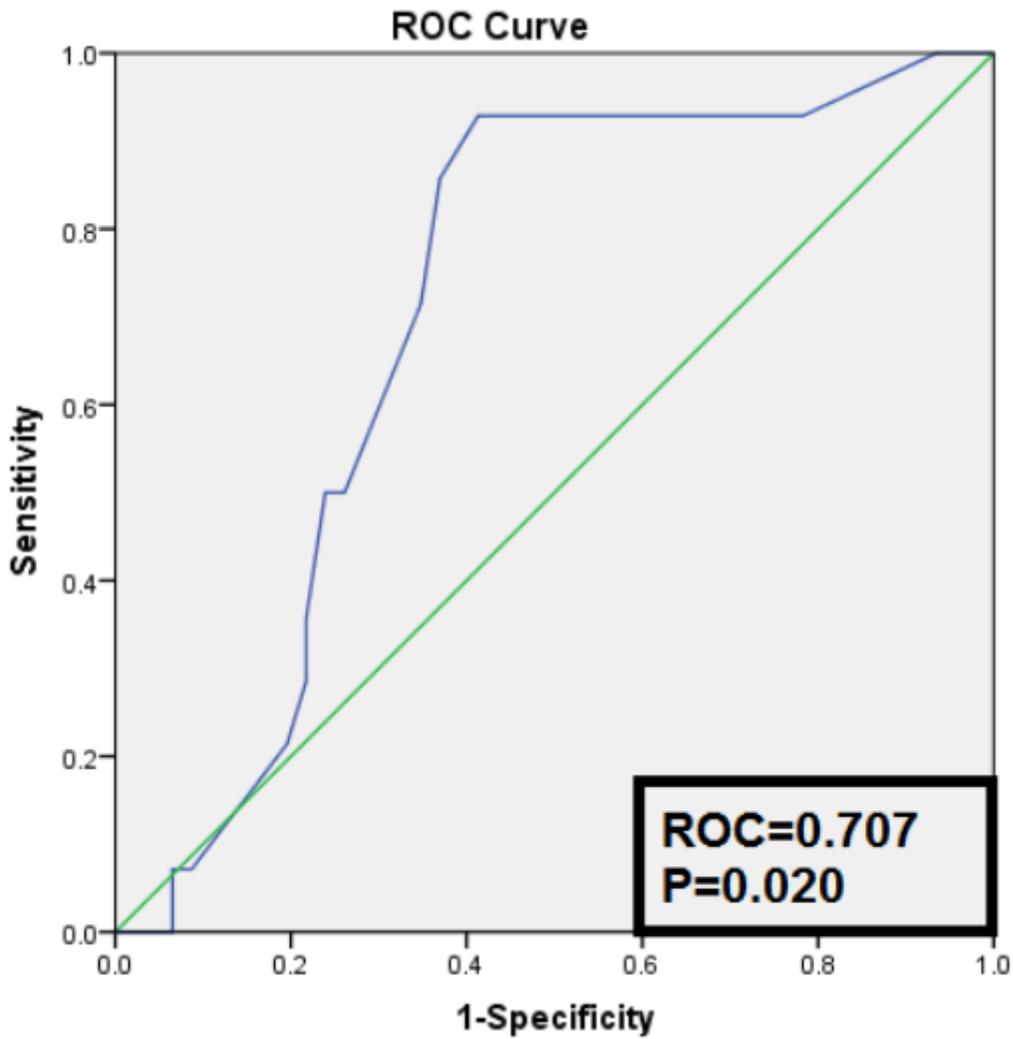


Figure 3

ROC curve of course of hypertension to distinguish remission group from non-remission group.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [LedeLinSupplementTable1.pdf](#)