## **ORIGINAL ARTICLE**

## Efficacy of Prophylactic Embolisation of Renal Angiomyolipomas Using Semi-automatic Segmentation for Volume Measurement

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#### **ABSTRACT**

**Introduction:** We aimed to assess the efficacy of prophylactic embolisation of renal angiomyolipomas (AMLs) by determining post-embolisation rupture risk, as well as changes in total volume and in angiomyogenic and fatty components using semi-automatic segmentation.

Methods: This was a retrospective study of 22 adult patients with prophylactic embolisation of AML performed between January 2009 and January 2024. Patients were followed up for any post-embolisation rupture. Pre- and post-embolisation computed tomography (CT) data were assessed using the open-source software 3D Slicer for semi-automatic segmentation. Volumetric changes of AMLs were compared using the Wilcoxon signed-rank test for paired data and Mann-Whitney U test for unpaired data. Spearman's rank correlation coefficient was used to identify any associations between variables.

**Results:** There were 25 prophylactic embolisations performed on the 22 adult patients with AML (18 females [81.8%]), with a median age of 60.0 years (interquartile range [IQR], 15.0). No procedure-related complications were encountered. The median follow-up was 49.0 months (IQR, 56.0) with no post-embolisation rupture. Pre- and post-treatment median tumour volumes were 67.5 cm³ (IQR, 116.1) and 35.7 cm³ (IQR, 82.1), respectively. There was a significant reduction in total tumour volume (41.4%), including angiomyogenic (73.6%) and fatty components (14.0%) [all p < 0.001]. Factors associated with greater tumour volume reduction included a higher proportion of angiomyogenic and a lower proportion of fatty components (both p < 0.001).

**Conclusion:** Prophylactic embolisation of AML effectively reduced tumour volume, with more significant changes in its angiomyogenic than fatty components. No post-embolisation rupture was documented with a median follow-up of over 4 years.

Key Words: Angiomyolipoma; Embolization, therapeutic; Hemorrhage; Kidney neoplasms; Tumor burden

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## 中文摘要

## 半自動分割體積測量法評估預防性栓塞治療腎血管平滑肌脂肪瘤的療效

林栢麟、吳昆倫、李家灝、馮建勳、曹慶恩

**引言:**釐本研究旨在透過半自動分割技術,評估腎血管平滑肌脂肪瘤(AML)預防性栓塞的療效, 具體方法包括確定栓塞術後破裂風險以及腫瘤總體積、血管肌源性成分和脂肪成分的變化。

方法:本研究為回顧性研究,納入2009年1月至2024年1月期間接受AML預防性栓塞的22位成年患者。所有患者均接受隨訪,觀察栓塞術後是否發生破裂。我們採用開源軟件3D Slicer對栓塞術前及術後的電腦斷層掃描圖像進行半自動分割,並採用Wilcoxon 符號排序檢定(配對資料)和Mann-Whitney U 檢定(非配對資料)比較AML的體積變化,以及採用Spearman秩相關系數分析各變數間的相關性。

**結果**:22位成年AML患者(18位女性[81.8%])接受了25次預防性栓塞治療,中位年齡為60.0歲(四分位數間距[IQR]為15.0)。沒有發生手術相關併發症。中位隨訪時間為49.0個月(IQR為56.0),沒有發生栓塞後破裂。治療前後腫瘤體積中位數分別為67.5 cm³(IQR為116.1)及35.7 cm³(IQR為82.1)。腫瘤總體積顯著縮小(41.4%),其中血管肌源性成分縮小73.6%,脂肪成分縮小14.0% [所有p < 0.001]。腫瘤體積顯著縮小的相關因素包括血管肌源性成分比例較高和脂肪成分比例較低(兩者 p < 0.001)。

**結論**:預防性栓塞治療AML可有效縮小腫瘤體積,且血管肌源性成分的變化比脂肪組成的變化更為顯著。中位隨訪時間超過4年,未記錄到栓塞後破裂病例。

#### INTRODUCTION

Renal angiomyolipoma (AML) is the most common benign solid renal tumour. The majority (approximately 80%) occur sporadically, while the rest (approximately 20%) are associated with phakomatoses, most commonly tuberous sclerosis. AML belongs to the family of tumours with perivascular epithelioid cellular differentiation. It typically contains both angiomyogenic and fatty components, with the latter readily identifiable in computed tomography (CT) due to its hypoattenuating nature (< -10 Hounsfield unit [HU]) [Figure 1]. A.5

It is well recognised that AML carries a risk of rupture with bleeding, especially for larger tumours, which can lead to fatal consequences. Treatment options include transcatheter arterial embolisation and radiofrequency ablation, as well as partial or radical nephrectomy. Selective arterial embolisation can be performed in an emergency setting for AML with active bleeding. It can also be a prophylactic treatment to reduce tumour size and its risk of haemorrhage (Figure 1). It has been suggested that for AML of 4 cm or above in diameter, or those with microaneurysms 0.5 cm or above in the feeding artery, prophylactic selective arterial embolisation is

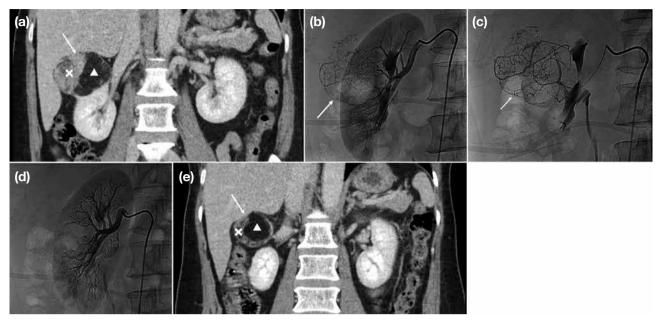
indicated.<sup>11</sup> Different embolisation agents have been reported in the literature, including microparticles, such as microspheres, and liquid agents, such as ethanol. Past studies have shown that prophylactic embolisation could reduce the size of AML, thus reducing its haemorrhagic risk.<sup>9,10,12</sup> In addition, the risk of haemorrhage is mainly attributed to the angiomyogenic component of AML.<sup>13-15</sup> Yet, there are limited studies accurately assessing how tumour composition changes after treatment.

For AML, tumour size has been shown to be associated with risk of spontaneous rupture, with larger ones more likely to bleed.<sup>6,7,11</sup> This study therefore aimed to assess the efficacy of prophylactic selective arterial embolisation in determining the rupture risk postembolisation and reducing the volume of AML using semi-automatic segmentation as a measurement tool. Changes in its angiomyogenic and fatty components were also evaluated.

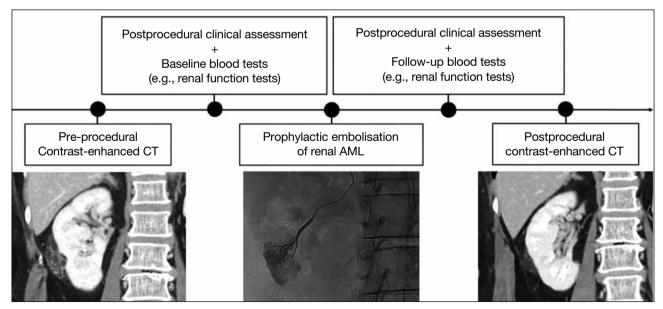
## **METHODS**

#### **Patient Selection**

This was a single-centre, single-arm retrospective study. Consecutive adult patients (≥18 years old) who



**Figure 1.** Renal angiomyolipoma (AML) pre- and post-prophylactic embolisation. (a) Pre-procedural contrast-enhanced computed tomography (CT) of the abdomen with coronal reformation shows an exophytic mass arising from the upper pole of the right kidney containing both soft tissue (cross) and fat (triangle) components, suggestive of an AML (arrow). (b) Pre-embolisation catheter angiogram demonstrates hypervascular nature of the AML (arrow) with tortuous vessels. (c) Selective catheter angiogram via microcatheter identifies the feeding artery of the AML (arrow), allowing targeted deployment of embolisation agent. (d) Post-embolisation catheter angiogram confirms technical success with complete resolution of tumour stain. (e) Postprocedural contrast-enhanced CT of the abdomen shows reduction in total volume of AML (arrow), with greater shrinkage of the angiomyogenic (cross) than fatty (triangle) components.



**Figure 2.** Protocol for prophylactic embolisation of renal angiomyolipoma. Abbreviations: AML = angiomyolipoma; CT = computed tomography.

underwent prophylactic embolisation of AML (Figure 2) in a public acute general hospital between January 2009 and January 2024 were included. Exclusion criteria included paediatric patients (<18 years old), patients who underwent emergency embolisation of ruptured AML, and patients without pre- or postprocedural CT.

#### **Data Collection**

Clinical data of the included patients were retrieved from the radiology information system of the hospital network. They included demographics and medical history, such as tuberous sclerosis status. Presenting symptoms and postprocedural complaints were recorded. Pre- and postintervention blood tests, such as haemoglobin level and renal function tests, were documented.

Details of prophylactic embolisation of AML were logged. They encompassed the type and amount of embolisation agents deployed, as well as catheters and guidewires used, which were chosen based on the operators' preference. Data on technical success, defined as complete angiographic resolution of tumour stain and microaneurysms, as well as contrast stasis of the feeding artery, were documented. Intraoperative and immediate postprocedural complications were recorded. Subsequent clinical follow-up was reviewed for postembolisation tumour rupture.

#### Radiological Assessment

Pre- and post-embolisation plain and contrast-enhanced CTs of the abdomen in DICOM (Digital Imaging and Communications in Medicine) format were obtained from the picture archiving and communication system of the hospital network. The time interval between the day of CT examination and interventional procedure was logged. DICOM images were assessed using 3D Slicer (macOS version 5.6.2; The Slicer Community), an open-source image computing platform.<sup>16</sup> Semiautomatic segmentation of AMLs was performed in the following sequence (Figure 3): (1) reformation of contrast-enhanced CT images in axial, coronal and sagittal planes; (2) manual contouring of tumour and non-tumour regions on limited CT slices (<5); (3) automatic segmentation of tumour and non-tumour regions using the 'grow from seeds' algorithm; (4) manual refinement of segmented regions using 'paint' and 'erase' algorithms; (5) automatic differentiation between angiomyogenic and fatty components of AML using a 'threshold' algorithm, with the threshold set at  $\geq$  -10 HU for the angiomyogenic component and < -10 HU for the fatty component; (6) automatic volume rendering of tumour and non-tumour regions; and (7) automatic volumetric computation of the entire AML, as well as its angiomyogenic and fatty components. In addition, laterality and polarity of AML, as well as the presence or absence of aneurysms, were documented. In postprocedural CT, any complications, including renal parenchymal infarction, haematoma, abscess, pyelonephritis, or hydronephrosis, were recorded.

#### **Statistical Analysis**

Statistical analysis was performed using SPSS (macOS version 29.0; IBM Corp, Armonk [NY], United States). The distribution of all numerical data was first tested for

normality using the Shapiro-Wilk test. The Wilcoxon signed-rank test was used to compare paired data, such as pre- and postprocedural volumetric changes in each AML. The Mann-Whitney U test was used for comparison between unpaired data. Spearman's rank correlation coefficient was used to identify association between variables. A p value of < 0.05 was considered statistically significant.

This manuscript was prepared in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

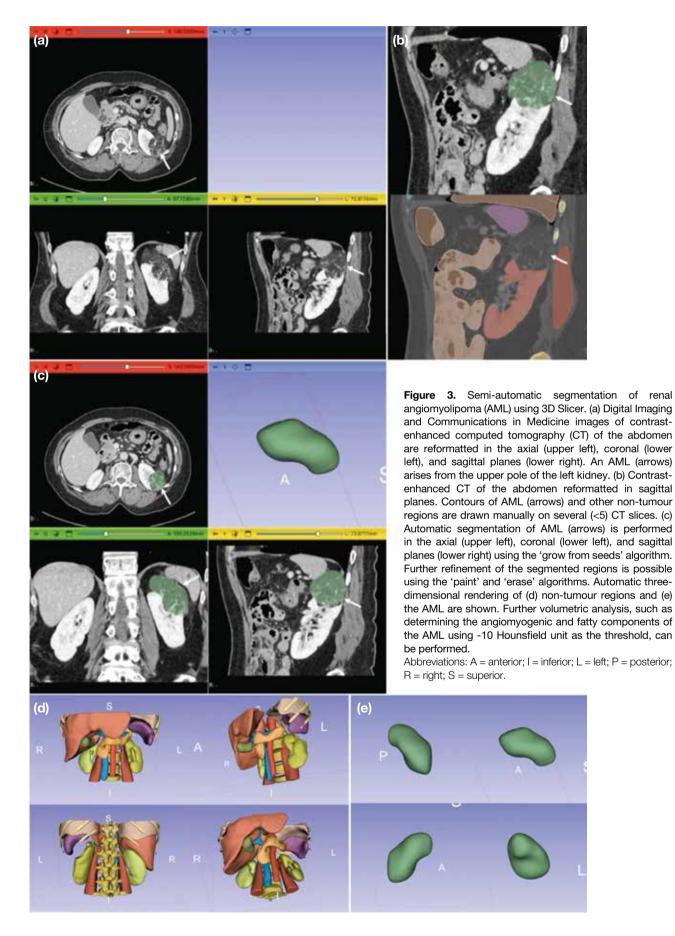
#### RESULTS

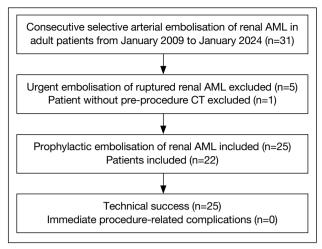
#### **Patient Demographics and Clinical Information**

There were 31 prophylactic embolisations of AMLs in adult patients performed from January 2009 to January 2024. Five patients underwent emergent embolisation of ruptured AMLs. One patient did not have preoperative CT available for assessment. These six patients were therefore excluded. A total of 25 prophylactic embolisations of AML in 22 patients were finally included in the study, of which three patients had repeated embolisation (n = 3, 13.6%) [Figure 4]. The median age of the patients on the day of embolisation was 60.0 years (interquartile range, 15.0). Most patients were female (n = 18, 81.8%). There was no patient with tuberous sclerosis. Four patients (18.2%) had known chronic kidney disease due to diabetic nephropathy (n = 2, 9.1%), hypertensive nephropathy (n = 1, 4.5%)and IgA nephropathy (n = 1, 4.5%) [Table 1].

# Prophylactic Embolisation of Renal Angiomyolipoma

All prophylactic embolisations of AMLs were performed due to large tumour size (≥4 cm in diameter). In one case (4.0%), there was a 0.5-cm aneurysm identified in pre-procedural assessment, which was successfully embolised. Microspheres (Embosphere Microsphere; Merit Medical Systems, South Jordan [UT], United States) were employed in two-thirds of all interventions (n = 17, 68.0%). The sizes of the microparticles ranged between 100-300  $\mu$ m (n = 2, 11.8%), 300-500  $\mu$ m (n = 6, 35.3%) and 500-700  $\mu m$  (n = 9, 52.9%). Ethanol was used in the remaining one-third of the cases (n = 8)32.0%). Ethanol was radio-opacified with ethiodised oil in a ratio of 7:3 for embolisation of the other cases. Selective arterial embolisation with microcatheters and microguidewires was performed in every case. All prophylactic embolisation achieved technical





**Figure 4.** Selection of study population with prophylactic embolisation of renal angiomyolipoma.

Abbreviations: AML = angiomyolipoma; CT = computed tomography.

**Table 1.** Demographics and clinical information of the study population.\*

Age at embolisation, y (n = 25)	60.0 (15.0)
Sex (n = 22)	
Female	18 (81.8%)
Male	4 (18.2%)
Tuberous sclerosis status (n = 22)	0
Medical history (n = 22)	
Diabetic nephropathy	2 (9.1%)
Hypertensive nephropathy	1 (4.5%)
IgA nephropathy	1 (4.5%)

<sup>\*</sup> Data are shown as No. (%) or median (interquartile range).

success. There were no intra-procedural or immediate postprocedural complications encountered. The median time intervals between pre- and postprocedural CT with prophylactic embolisation were 90.0 days and 107.0 days, respectively. Postprocedural CT showed a small (2.0 cm in diameter) subsegmental renal infarction in one case (4.0%). No other complications were seen. There were no significant changes in haemoglobin level or renal function tests before and after prophylactic embolisation. Median clinical follow-up duration was over 4 years (49.0 months), with a minimum of 6 months. There were no post-embolisation rupture of AML (Table 2).

## Volumetric Analysis of Renal Angiomyolipoma

The median total volume of AMLs in pre- and postprocedural CTs were 67.5 cm<sup>3</sup> and 35.7 cm<sup>3</sup>, respectively, showing significant interval shrinkage,

**Table 2.** Details of prophylactic embolisation of renal angiomyolipoma (n = 25).\*

Pre-procedural assessment	
Interval between pre-procedural CT and	90.0 (144.0)
embolisation, d	
Laterality of AML	
Right kidney	19 (76%)
Left kidney	6 (24%)
Polarity of AML	
Upper pole	10 (40%)
Interpolar region	2 (8%)
Lower pole	11 (44%)
Entire kidney involved	2 (8%)
AML-associated aneurysm	1 (4%)
Baseline blood tests	, ,
Haemoglobin level, g/dL	13.1 (1.7)
Normal renal function tests	21 (84%)
Prophylactic embolisation of AML	_: (=:,-,
Indication for embolisation (AML ≥4 cm in	25 (100%)
diameter)	_= (,
Embolisation agent	
Microspheres, µm	17 (68%)
100-300	2 (11.8%)
300-500	6 (35.3%)
500-700	9 (52.9%)
Ethanol	8 (32%)
Microcatheter and microguidewires employed	25 (100%)
Technical success	25 (100%)
Intra-procedural or immediate postprocedural	0
complications	
Postprocedural assessment	
Interval between postprocedural CT and	107.0 (45.0)
embolisation, d	, ,
Residual AML-associated aneurysm	0
Complications	
Renal parenchymal infarction	1 (4%)
Haematoma	0 '
Abscess	0
Pyelonephritis	0
Hydronephrosis	0
Follow-up blood tests	
Haemoglobin level, g/dL	12.9 (2.5)
Normal renal function tests	21 (84%)
Duration of clinical follow-up, mo	49.0 (56.0)
Post-embolisation rupture	0
Alabama daliana ANAI anniana alimana CT	

Abbreviations: AML = angiomyolipoma; CT = computed tomography.

with 41.4% total tumour volume reduction. Both angiomyogenic and fatty components showed significant interval reduction in size, attaining 73.6% and 14.0% volume loss, respectively. The angiomyogenic component of the AMLs showed significantly greater reduction in size compared to the fatty component (Table 3).

<sup>\*</sup> Data are shown as No. (%) or median (interquartile range).

<sup>&</sup>lt;sup>†</sup> One pre-procedural AML-associated aneurysm was present (0.5 cm in diameter), which was successfully embolised.

<sup>&</sup>lt;sup>‡</sup> Four patients with known chronic kidney disease; their pre- and postprocedural renal function tests showed no significant change.

Table 3. Compositions of renal angiomyolipoma before and after prophylactic embolisation (n = 25).

	Pre-procedural volume, cm <sup>3</sup>	Postprocedural volume, cm <sup>3</sup>	Volume reduction	p Value
Total AML	67.5 (116.1)	35.7 (82.1)	41.4% (40.8%)	< 0.001
Angiomyogenic component	12.2 (29.5)	2.9 (5.0)	73.6% (31.9%)	< 0.001
Fatty component	46.9 (103.4)	31.3 (75.5)	14.0% (29.8%)	< 0.001
Comparison of volume reduction of angiomyogenic versus fatty component				< 0.001

Abbreviation: AML = angiomyolipoma.

**Table 4.** Correlation analysis performed to identify factors associated with total angiomyolipoma volume reduction after prophylactic embolisation (n = 25).

	Spearman's rho (if applicable)	p Value
Demographics and clinical factors		
Age	0.066	0.755
Sex (female vs. male)	N/A	0.447
Baseline blood tests		
Haemoglobin level	0.221	0.288
Renal function (normal vs. abnormal)		
Pre-procedural AML characteristics		
Laterality (right kidney vs. left kidney)	N/A	0.092
Diameter	-0.146	0.486
Total volume	-0.165	0.432
Proportion of angiomyogenic	0.674	< 0.001
component		
Proportion of fatty component	-0.657	< 0.001
Procedure-related factors		
Embolisation agent (microsphere vs. ethanol)	N/A	0.262

Abbreviations: AML = angiomyolipoma; N/A = not applicable.

Correlation analysis revealed AMLs with a greater proportion of angiomyogenic component and smaller proportion of fatty component in pre-procedural CT were associated with greater tumour volume reduction after prophylactic embolisation. No other clinical or procedural factors associated with total tumour shrinkage were identified (Table 4).

Prophylactic embolisation of AML with either microspheres or ethanol achieved significant reduction in total tumour size, with 26.2% (p < 0.001) and 42.7% (p = 0.008) volume loss, respectively. Using either embolisation agent, there were significant reduction in volume of both angiomyogenic (microspheres: 71.6%, p < 0.001; ethanol: 81.0%, p = 0.008) and fatty components (microspheres: 12.7%, p < 0.001; ethanol: 29.7%, p = 0.008), with the angiomyogenic component

showing significantly greater volume loss than the fatty component using either embolisation agent (both p < 0.001). Comparing microspheres and ethanol, there were no statistically significant differences in their efficacy of reduction of the total tumour volume, angiomyogenic or fatty components of AML (Table 5).

#### DISCUSSION

Transcatheter embolisation of AML is recognised as a safe intervention. Ompared to more invasive treatment options such as partial or radical nephrectomy, transcatheter selective arterial embolisation typically only requires local anaesthesia, has lower risks of bleeding and infection, and allows shorter admission times. Some authors therefore suggest transcatheter embolisation as the first-line treatment option. In our study, no intra-procedural or immediate complications were encountered. However, in one patient, a small subsegmental renal infarction was seen in postprocedural CT. This highlights the importance of follow-up imaging, which encompasses assessment of treatment efficacy, as well as identification of complications.

There was significant change in tumour volume after prophylactic embolisation of AML, achieving over 40% reduction in median total volume amongst our study population. With decreased tumour volume, the risk of spontaneous haemorrhage would be lowered.<sup>6,11</sup> It was reassuring that none of the included patients encountered post-embolisation tumour rupture in clinical follow-up with a median duration of over 4 years. These findings demonstrate that prophylactic embolisation of AML is a safe and effective means to reduce haemorrhagic risk, concurrent with previous studies.<sup>9,10</sup>

Various materials for prophylactic embolisation of the kidney have been suggested in the literature, with microspheres and ethanol being two of the most commonly adopted agents. In this study, both

<sup>\*</sup> Data are shown as median (interquartile range).

Table 5. Efficacy of employing microspheres versus ethanol in prophylactic embolisation of renal angiomyolipoma.\*

	Pre-procedural volume, cm <sup>3</sup>	Postprocedural volume, cm <sup>3</sup>	Volume reduction	p Value
Total AML	79.8 (105.7)	53.1 (76.9)	26.2% (37.5%)	< 0.001
Angiomyogenic component	12.2 (27.4)	4.5 (4.3)	71.6% (29.9%)	< 0.001
Fatty component	57.3 (91.4)	50.4 (73.3)	12.7% (29.0%)	< 0.001
Comparison of volume reduction of angiomyogenic versus fatty component				< 0.001
Compositions of AML before and after prophy	vlactic embolisation with	ethanol as embolisation a	gent (n = 8)	
	Pre-procedural volume, cm <sup>3</sup>	Postprocedural volume, cm <sup>3</sup>	Volume reduction	p Value
Total AML	50.0 (192.5)	26.6 (112.6)	42.7% (35.2%)	0.008
Angiomyogenic component	15.0 (87.9)	1.9 (34.2)	81.0% (29.5%)	0.008
Fatty component	33.1 (101.0)	20.7 (74.2)	29.7% (38.5%)	0.008
Comparison of volume reduction of angiomyogenic versus fatty component				< 0.001
Comparison of AML compositions after proph	ylactic embolisation wit	n microspheres versus eth	anol (n = 25)	
		Microspheres (n = 17)	Ethanol (n = 8)	p Value
Total AML volume loss		26.2% (37.5%)	42.7% (35.2%)	0.262
Volume loss in angiomyogenic component		71.6% (29.9%)	81.0% (29.5%)	0.110
Volume loss in fatty component		12.7% (29.0%)	29.7% (38.5%)	0.086

Abbreviation: AML = angiomyolipoma.

microspheres and ethanol effectively reduced the size of AMLs by over 25%, without a statistically significant difference between the two agents. To the best of our knowledge, there is no large-scale study establishing whether microspheres or ethanol is the superior prophylactic embolisation agent for AML.<sup>9,10,12</sup> In our centre, this choice depended on the operators' preference.

It has been proposed that the effectiveness of prophylactic embolisation in achieving volume reduction depends on the composition of the AML, which has variable angiomyogenic and fatty components. The angiomyogenic component usually demonstrates greater response to embolisation due to its vascular nature, whereas the fatty component is hypovascular and more treatment-resistant. 9,17 A study by Han et al 17 showed near-complete resolution of the angiomyogenic component after prophylactic embolisation, but the fatty component only partially shrank. In their study, the proportion of angiomyogenic and fatty components were evaluated on a transverse image at the middle of the tumour. However, this might not reflect the actual composition of the entire AML. In our study, semi-automatic segmentation was performed, and the angiomyogenic and fatty components were differentiated using -10 HU as the threshold. This allowed a more

accurate volumetric assessment of AML. Similar to prior studies, there was significantly greater reduction in the angiomyogenic component than the fatty component after embolisation.

AMLs with a greater proportion of angiomyogenic component and smaller proportion of fatty component are associated with greater total volume reduction after embolisation. For AML with high fatty content, patients and clinicians may be concerned that about the smaller postprocedural volume reduction. However, the angiomyogenic component of AML, which is the main culprit in haemorrhage, has shown good response to embolisation.<sup>9,17</sup> In our study, the angiomyogenic component achieved over 70% volume reduction, which could be reassuring to both patients and clinicians.

#### Limitations

First, none of the patients in our study had tuberous sclerosis. Treatment efficacy for sporadic and tuberous sclerosis—associated AML may differ and have not been explored. Second, there was a lack of a control group to compare rupture risk in patients who received prophylactic embolisation versus those who did not. A double-arm study could better assess treatment effect. Third, the sample size was limited. This may be partly

<sup>\*</sup> Data are shown as median (interquartile range).

attributed to the relatively low prevalence of AML, which is below 0.5% in the population.<sup>18</sup> A multi-centre study with larger sample sizes is a potential future direction.

#### CONCLUSION

Prophylactic embolisation of AML effectively reduced tumour volume, with more significant changes in the angiomyogenic component compared to the fatty component. No rupture or haemorrhage was documented post-embolisation with a median follow-up of over 4 years.

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