ELSEVIER

Canadian Association of Radiologists Journal xx (2018) 1−4

CANADIAN ASSOCIATION OF RADIOLOGISTS JOURNAL

www.carjonline.org

Critically Appraised Topic / Évaluation critique

# What Are the Indications for Prophylactic Embolization of Renal Angiomyolipomas? A Review of the Current Evidence in the Literature

James W. Ryan, BSc (Hons) CPC, MB, BCh, BAO, MRCPI*,
Cormac Farrelly, MB, BCh, BAO, MSc (Hons), MRCPI, FFR RCSI,
Tony Geoghegan, MB(Hons), MSc, MRCPI, MRCOG, FFRRCSI, EBIR

*Department of Radiology, Mater Misericordiae University Hospital, Dublin, Ireland*

**Abstract**

Renal angiomyolipomas (AMLs) are benign tumours that may occur sporadically in the general population or in patients with tuberous sclerosis complex. The concern with AMLs is that of retroperitoneal hemorrhage, which can be fatal. Classically the trigger for prophylactic intervention was thought to be an AML diameter of ≥4 cm. However, this value is largely based on data from case series and heterogeneous retrospective studies. The PICO (patient, intervention, comparison, outcome) paradigm was used to systematically search the Cochrane database, TRIP database, and PubMed. The quality of evidence in the literature is poor regarding the indications for prophylactic embolization of AMLs (level 4). There are no prospective studies that adequately assess embolization vs other treatment modalities. However, using the available evidence we have produced recommendations for when intervention should be considered. We have also made recommendations regarding the direction of future research.

**Résumé**

Les angiomyolipomes sont des tumeurs bénignes du rein qui peuvent se manifester de façon sporadique au sein de la population ou chez des patients atteints de sclérose tubéreuse de Bourneville. Les angiomyolipomes posent un risque d'hémorragie rétropéritonéale pouvant être mortelle. L'intervention prophylactique était depuis longtemps fondée sur un diamètre de l'angiomyolipome supérieur ou égal à 4 cm. Cette valeur repose cependant en grande partie sur des données issues de séries de cas et d'études rétrospectives hétérogènes. Le paradigme PICO (patient, intervention, comparaison, résultat) a été utilisé pour effectuer une recherche systématique dans les bases de données Cochrane, TRIP et PubMed. La documentation scientifique contient peu de données probantes de qualité en ce qui a trait aux indicateurs de l'embolisation prophylactique des angiomyolipomes (niveau 4). Il n'existe pas non plus d'études prospectives qui évaluent adéquatement l'embolisation par rapport à d'autres modalités de traitement. Nous avons cependant pu formuler des recommandations à partir des données probantes disponibles pour déterminer à quel moment une intervention doit être envisagée. Nous avons également fait des recommandations en vue d'orienter de futurs travaux de recherche.



*Key Words:* Angiomyolipoma; Renal; Embolization; Prophylactic; Indication

## Clinical Problem

What are the indications for prophylactic embolization of renal angiomyolipomas?

## Research Question

In patients with renal angiomyolipomas (AMLs), when should prophylactic embolization be considered?

The PICO paradigm was used to systematically search the Cochrane database, TRIP database, and PubMed [1−3]. English language and human search filters were used. This search was carried out in November 2016. Retrieved abstracts were reviewed; relevant articles were then critically appraised using Oxford Centre for Evidence-Based Medicine

* Address for correspondence: James W. Ryan, BSc (Hons) CPC, MB, BCh, BAO, MRCPI, Department of Radiology, Mater Misericordiae University Hospital, Eccles Street, Dublin 7, Ireland.

*E-mail address:* jwryan@mater.ie (J. W. Ryan).

0846-5371/$ - see front matter 
https://doi.org/10.1016/j.carj.2018.01.002

Table 1
Summary of evidence base

| Author | Year | Aim | Study design | Level of evidence | Patients |
|---|---|---|---|---|---|
| Yamakado et al [9] | 2002 | To evaluate the relationship among AML aneurysms, AML size, and the risk of hemorrhage | Single-institution retrospective review | 4 | 20 sporadic, 3 TSC |
| Ouzaid et al [10] | 2014 | To present outcomes of AML patients undergoing AS and identify clinical features that were predictive of failed AS | Single-institution retrospective review | 4 | 120 sporadic, 10 TSC |
| Bissler et al [11] | 2016 | To compare MTORI to embolization in TSC AMLs | Systematic review | 4 | 125-132 TSC |
| Kuusk et al [7] | 2015 | To evaluate the effect of baseline characteristics and treatment methods on outcomes of sporadic AMLs | To evaluate the effect of baseline characteristics and treatment methods on outcomes of sporadic AMLs | 4 | 441 sporadic |
| Bhatt et al [8] | 2016 | To determine growth rates of untreated AMLs | Retrospective single-centre database review | 4 | 427 sporadic, 17 TSC |
| Sasongko et al [15] | 2016 | To evaluate the efficacy of MTORI vs placebo in TSC AMLs | Cochrane review article including data from 2 pertinent randomized, double-blind placebo-controlled trials | 1a | 235 TSC |

AML = angiomyolipoma; AS = active surveillance; MTORI = mammalian target of rapamycin inhibitor; TSC = tuberous sclerosis complex.

criteria and assigned a level of evidence [4,5]. The most robust, up-to-date articles containing the largest bodies of evidence were included.

## Evidence

### *Sporadic AMLs*

Please refer to Table 1 for information regarding study design, patient population and level of evidence for the following studies.

The prevalence of sporadic AMLs in a study including 61,389 patients was found to be 0.44%. AMLs were twice as common in women, and 0.4% of sporadic AMLs bled. The mean sporadic AML size was 1.1 cm [6].

### *Kuusk et al*

Patients presenting with bleeding AMLs (54 of 441) had significantly larger tumours than did those who did not present with bleeding ($P < .001$) [7] (Figure 1). A total of 128 of 441 patients underwent embolization, and of these 25% (32 of 128) presented with a retroperitoneal bleed. A total of 29.7% (38 of 128) required reintervention during follow-up ($P = .003$). The mean follow-up period was 44.5 ± 35.8 months. The reasons for reintervention were not specified.

### *Bhatt et al*

A total of 91% (424 of 471) of AMLs did not grow or grew slowly over follow-up [8]. The median follow-up period was 43 months (14-144 months). There was no significant difference between the average growth rate of AMLs <4 cm compared with AMLs >4 cm (0.002 cm/year; 95% confidence interval [CI]: −0.017 to 0.02; $P = .86$).

A total of 9% (41) of AMLs grew at an increased rate of ≥0.25 cm per year. These AMLs had a higher intervention rate ($P = .03$).

### *Yamakado et al*

A small group of 23 AML patients was reviewed [9]. Eight of 23 AMLs bled. AML aneurysm size was found to be a more accurate predictor of hemorrhage than AML diameter. Using an AML aneurysm size of >5 mm as a predictor of hemorrhage had 100% sensitivity and 86% specificity.

### *Ouzaid et al*

A total of 130 AML patients underwent active surveillance (AS); 13% (17 of 130) failed AS [10] (Figure 2). Two significant predictors of failed AS were identified: 1) symptoms at presentation (hazard ratio: 3.745; 95% CI: 1.412 to 9.9, $P = .008$); and 2) AML size >4 cm (hazard ratio: 11.23; 95% CI: 3.412 to 37.03; $P = .001$).

Importantly, the authors found that prophylactic embolization of all AMLs >4 cm would have resulted in an over treatment rate of 65% at a mean ± SD follow-up of 49 ± 40 months. Thirteen of the 38 patients with an AML size >4 cm failed AS. The reasons for failed AS within this subgroup were not specified. 67.8% (19 of 28) of symptomatic patients

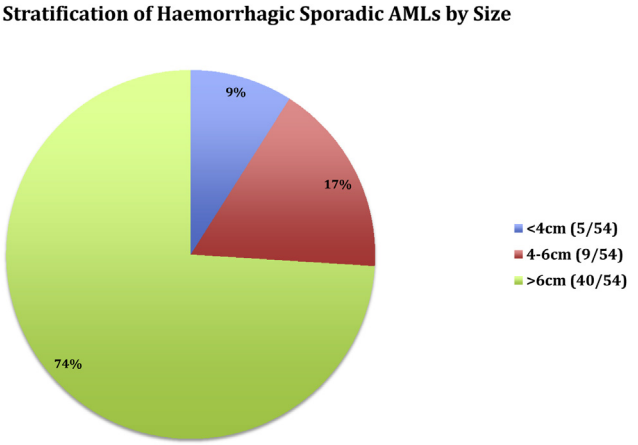


Figure 1. Stratification of hemorrhagic sporadic AMLs by size [7]. AML = angiomyolipoma.