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# Thèse

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Diplôme d'État

Par


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## Facteurs de risques de complications après embolisation des artères utérines pour fibromes symptomatiques : existent-ils ?

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# SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté,
de mes chers condisciples
et selon la tradition d'Hippocrate,
je promets et je jure d'être fidèle aux lois de l'honneur
et de la probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuits à l'indigent,
et n'exigerai jamais un salaire au-dessus de mon travail.

Admis dans l'intérieur des maisons, mes yeux
ne verront pas ce qui s'y passe, ma langue taira
les secrets qui me seront confiés et mon état ne servira pas
à corrompre les mœurs ni à favoriser le crime.

Respectueux et reconnaissant envers mes Maîtres,
je rendrai à leurs enfants
l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime
si je suis fidèle à mes promesses.
Que je sois couvert d'opprobre
et méprisé de mes confrères
si j'y manque.

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## Abbreviations

| | |
|---|---|
| BMI | Body mass index |
| cc | Cubic centimeter/Centimètre cube |
| CCAM | Classification Commune des Actes Médicaux |
| CHU | Centre hospitalo-universitaire |
| CIM-10 | Classification Internationale des Maladies, 10° édition |
| CNGOF | Collège National des Gynécologues et Obstétriciens Français |
| cm | Centimeters/Centimètres |
| CNIL | Commission Nationale de l'Informatique et des Libertés |
| DIU | Dispositif intra-utérin |
| EAU | Embolisation des artères utérines |
| FIGO | Fédération internationale de gynécologie et obstétrique |
| HIFU | High Intensity Focalized Ultrasounds |
| HIV | Human Immunodeficiency Virus |
| HR | Hazard ratio |
| HSC | Hysteroscopy/Hystéroscopie |
| HST | Hysterectomy/ Hystérectomie |
| IC 95% | Confidence interval of 95% |
| IMC | Index de masse corporelle |
| IRM | Imagerie par résonance magnétique |
| IT | Information technology |
| IUD | Intra-uterine device |
| IV | Intravenous |
| m | Mean |

| | |
|---|---|
| mL | Milliliters/Millilitres |
| MRI | Magnetic Resonance Imaging |
| n | Number |
| NA | Not applicable/Non applicable |
| OR | Odd's ratio |
| PACS | Picture archiving and communication system |
| PVA | Polyvinyl alcohol particles |
| SCGC | Society of Obstetricians and Gynecologists of Canada |
| SD | Standard Deviation |
| SIMEES | Service d'Information Médicale, Epidémiologie et Economie de la Santé |
| SIR | Society of Interventional Radiology Standards of Practice Committee |
| UAE | Uterine Artery Embolization |

## Résumé

INTRODUCTION L'embolisation des artères utérines (EAU) est réputée comme une alternative sûre et efficace à la chirurgie pour traiter les fibromes symptomatiques. Les facteurs de risques de complication ne sont pas clairement identifiés dans la littérature.

METHODES Nous avons réalisé une étude cas-témoins sur les dernières 15 années dans notre centre universitaire spécialisé. Toutes les complications au minimum de grade 2 selon les recommandations pour la pratique de la société de radiologie interventionnelle, correspondant à des complications sévères ou nécessitant une hospitalisation ont été colligées.

RESULTATS Parmi les 73 cas recensés, 24,7% ont été hospitalisés pour douleurs (n=18/73), 26% pour infection (n=19/73) et 2,74% ont expulsé leur fibrome (n=2/73). Au total, 35 patients ont eu recours à une deuxième ligne de traitement (47,9%), plus souvent chirurgical (n=18/35, 51,4%). L'analyse univariée (n=69) isolait l'immunosuppression (p=0,02), l'association DIU avec adénomyose (p=0,04), le volume du plus gros fibrome (p=0,04), la localisation sous-muqueuse d'un fibrome (p<0,01), l'estimation du volume utérin (p<0,01), le type et la quantité de particules utilisées (p=0,03) comme facteurs de risques potentiels. Seule la localisation sous-muqueuse (OR=4,84, IC95%=[1,95; 12,03], p<0,01) était indépendamment liée aux complications des EAU.

CONCLUSION Le seul facteur de risque indépendant de complication d'embolisation des artères utérines retrouvé est la présence de fibrome sous-muqueux (p<0,01). Il doit être pris en considération pour informer les patients, mettre en place leur surveillance et les conseiller sur de potentielles alternatives thérapeutiques.

# Résumé substantiel


## INTRODUCTION

Environ un tiers de la population féminine souffre de fibrome utérin. (1) L'embolisation des artères utérines (EAU) est un traitement conservateur recommandé, de nos jours pour les fibromes uniques de moins de 10 cm ou les fibromes multiples d'une quinzaine de centimètres. (2) (3) L'EAU a un taux de complications faible. (4) (5) La complication la plus fréquente est l'échec du traitement, menant à une seconde ligne thérapeutique. (6) (7) (8) Malheureusement, certaines complications peuvent être vitales ou altérer la qualité de vie des patientes de manière définitive, notamment l'infection. (9) (10) Ces complications sont rares; seuls quelques case reports sont retrouvés dans la littérature. (11) (12) Les études rétrospectives suggèrent que la taille et la localisation des fibromes utérins seraient un facteur de risque de complications. (13) Récemment, une étude cas témoins rapporte le volume utérin et l'IMC comme facteurs de risque d'infection. (14) Ces facteurs de risque ne sont pas clairement identifiés à ce jour. Et leur recherche est limitée par la faible incidence des complications. S'ils existent réellement, leur identification permettrait d'éviter certaines chirurgies réalisées en urgence pour complication.

En parallèle, une étude récente souligne les discordances entre les différentes recommandations au niveau international et demande une réflexion sur l'objectivité de chacune d'entre elles. (15)

Dans ce contexte, nous souhaitons réaliser une étude cas témoins cherchant à déterminer les facteurs de risque de complications sévères d'embolisation des artères utérines dans notre centre universitaire spécialisé.

## METHODES

1. Design

Nous avons réalisé une étude rétrospective cas témoins dans le centre hospitalier universitaire de Tours pour évaluer les facteurs de risque d'embolisation des artères utérines. Toutes les patientes ayant eu une EAU pour fibrome symptomatique, entre janvier 2005 et le premier juin 2020, étaient éligibles.

2. Critères d'inclusion

Pour les cas, toutes les patientes présentant au moins une complication sévère après EAU connues de l'hôpital étaient incluses.

Pour chaque cas, deux témoins étaient appariés sur le département d'habitation, l'âge et l'année d'embolisation étalonnés sur plus ou moins un an.

3. Critères d'exclusion

Les embolisations réalisées pour tout autre diagnostic que des fibromes ont été exclus. De même, si le diagnostic incluait des fibromes associés à une autre pathologie, les patientes étaient exclues de l'étude. L'embolisation des artères ovariennes était acceptée. Les complications spécifiques de procédure (par exemple vasculaire) n'étaient pas considérées. Les complications considérées mineures, ainsi que les hospitalisations pour un motif non relié à l'EAU, n'étaient pas incluses.

4. Collection des données

- Patientes

Les cas ont été recherchés avec l'aide du SIMEES, via plusieurs méthodes. Les différentes méthodes utilisées pour retrouver les cas ont été successivement : une méthode par mots clés dans tous les dossiers informatiques correspondant à des patientes hospitalisées ou consultant en gynécologie, une recherche rétrospective par le système de codage CCAM et CIM-10 correspondant aux actes d'EAU et diagnostics de fibromes utérins ainsi que les différentes complications possibles, un système de chainage entre EAU et hospitalisation ou consultation dans les 3 mois. Puis des cas ont été retrouvés en réalisant notre analyse des perdus de vues ainsi qu'en recueillant les potentiels témoins. Chez les patientes ayant recours à plusieurs l'EAU, la première procédure réalisée dans notre centre était prise en considération.

- Suivi

Les patientes ayant une EAU sont hospitalisées pour 24 à 48 heures post-procédure dans le service de gynécologie; puis une IRM de contrôle est programmée pour toutes les patientes 6-8 mois après l'intervention. De ce fait, les patientes vivant hors département, sont suivies au CHU.

- Complications

Seules les complications sévères nécessitant une hospitalisation, suivant la classification SIR, ont été considérées. (16) Les complications précoces étaient définies par une

survenue dans les trois mois post-embolisation. Elles étaient différenciées des complications tardives, diagnostiquées au-delà de trois mois après l'embolisation. L'infection et la douleur étaient incluses qu'en cas d'hospitalisation ou de nécessité d'un traitement intraveineux. Le syndrome post-embolisation a été inclus s'il nécessitait, lui aussi, une hospitalisation.

L'échec de traitement était défini par le recours à une nouvelle ligne de traitement : neuro-interventionnelle ou chirurgicale. S'il était peu symptomatique (pesanteur pelvienne, pollakiurie, métrorragies peu abondantes), l'échec de traitement était la complication considérée. Par contre en présence de symptômes sévères, l'échec de traitement était considéré symptomatique et le symptôme initial était considéré comme une complication selon les critères définis précédemment.

- Facteurs de risques

Tous les facteurs de risques retrouvés dans la littérature ont été pris en considération : IMC, tabagisme actif, présence d'un stérilet (DIU), fibrome sous-muqueux, types et taille de particules injectées, traitement additionnel ou infection connus lors de l'EAU. L'association DIU et adénomyose a été également étudiée comme un facteur de risque potentiel. L'IRM pelvienne était l'imagerie de référence pour évaluer le nombre de fibromes, la taille de l'utérus et des fibromes ainsi que le type FIGO des fibromes. Le volume utérin était calculé selon les équations de Shiota (Volume utérin= (longueur x largeur x profondeur x 0,35) + 107) et Harb (Volume utérin=longueur x hauteur x largeur x 0,52). (17) (18) De même, le volume du principal fibrome était estimé par une formule ellipsoïde. (19)

5. Statistiques

- Plan statistique

Le protocole de l'étude a été réfléchi et approuvé en amont par le département informatique et épidémiologique de notre hôpital.

Il a été prévu trois analyses :

-étude cas-témoin à la recherche de facteurs de risque de complications d'EAU

-recherche de prévalence des embolisations dans notre centre sur 15 ans

-étude des perdus de vue

- Analyses

Les analyses statistiques ont été réalisées avec le logiciel SPSS (version 20, IBM). Les variables quantitatives ont été testées via un test Z ou t de Student. Un risque $\alpha$ de 5%

pour un test bilatéral était considéré significatif. L'analyse univariée était réalisée par une analyse de corrélation linéaire. Les facteurs significatifs, avec p<0,20, en analyse univariée ont été considérés pour l'analyse multivariée. Les variables indépendantes ayant une incidence de 10 ou moins ont été exclues de l'analyse multivariée. (20) Une régression logistique binaire a été effectuée pour l'analyse multivariée.

- Etude rétrospective

Les systèmes de codage CCAM et CIM-10 ont été recoupés pour rechercher toutes les embolisations réalisées pour fibromes utérins dans les 15 dernières années. Puis la prévalence des patientes ayant réalisé une IRM 5 à 10 mois après l'embolisation a été recherchée pour évaluer le nombre de patientes réalisant l'IRM de contrôle prévue 6 à 8 mois après la procédure. Si aucune IRM n'était réalisée dans cet intervalle, les patientes étaient considérées comme perdues de vue.

6. CNIL

La CNIL a approuvé notre étude et collection de donnée en amont. Aucune autre autorisation éthique n'était nécessaire pour la réalisation de notre étude rétrospective.

## RESULTATS

1. Inclusion des patientes

Soixante-huit patientes ont été retrouvées via le système de mots clés. Par méthode de codage, 14 doublons ont été trouvés et 25 nouvelles patientes ont été incluses. Dix autres patientes ont été incluses grâce à la méthode de chainage. Un total de 103 patientes étaient alors éligibles, desquelles 43 ont été exclues. La recherche des perdus de vue a permis d'identifier 9 patientes incluables ; et l'identification des témoins a révélé 4 nouveaux cas. Une de ces patientes était déjà incluse dans l'étude. Au final, 73 patientes ont été incluses dans notre étude. (Figure 1)

2. Description de notre population

- Les cas

73 patientes entre 26 et 54 ans ont été incluses. Quatre patientes présentaient une immunosuppression : une polyarthrite rhumatoïde, une hypergammaglobulinémie et deux VIH en cours de traitement. Quatorze patientes avaient une longue histoire de fibromes, parmi elles, une avait eu recours à une ablation par ultrasons focalisés (HIFU). (Tableau 1) Vingt-et-une patiente ne prenaient aucun traitement à l'inclusion, mais cinq patientes s'automédiquaient par antalgiques ou anti-inflammatoire. Quatre patientes

prenaient des traitements au long cours pour des pathologies chroniques sans lien avec leurs fibromes. (Tableau 2)

- Les complications

Sur les 73 cas, 32 ont présenté une complication précoce. La principale complication présenté par les patientes était la douleur (n=18/73, 24,7%), une infection (n=19/73, 26%), dont un sepsis (n=7/73, 9,6%). L'échec de traitement isolé asymptomatic représentait 34,2% des complications (n=25/73). (Figure 2) Huit patientes présentant des complications précoces n'ont pas été hospitalisées dont trois avaient une infection confirmé sur prélèvement vaginal (n=3/73, 4,1%), 1 des métrorragies (n=1/73, 1,4%), 2 expulsaient leur fibrome (n=2/73, 2,7%), 1 autres une expulsion de fibrome surinfecté (n=1/73, 1,4%).

De nombreuses patientes se présentaient avec des symptômes variés (n=24/73, 32,9%). Quarante-et-une patientes ont présenté des complications tardives (n=41/73, 56,2%). (Figure 3) Celles-ci étaient en grande majorité des échecs de traitement (n=25/41, 61%). (Figure 4) Lors d'échec de traitement symptomatique, donc en présence de complications, les patients avaient plus recours à un second traitement chirurgical. (Figure 5)

Six expulsions asymptomatiques de fibrome ont été découvertes sur l'IRM de contrôle (4,3%).

- La population cas-témoins

Quatre cas n'avaient pas de témoins correspondant sur les trois critères d'appariement et n'ont donc pas été incluses dans l'étude cas-témoins.

3. Etude cas témoins

- Description de la population de l'étude cas-témoins

Aucun contrôle n'était immunodéprimé. Il existait une différence de prévalence d'immunodépression entre les deux groupes (p=0,02). Le groupe contrôle présentait plus de pathologies chroniques nécessitant des thérapeutiques au long cours principalement de l'hypertension, du diabète de type II, des dysthyroïdies ou des syndromes dépressifs (p<0,01). Les groupes étaient similaires sur les autres critères cliniques et thérapeutiques étudiés. (Tableau 3 et 4)

- Caractéristiques IRM

Le diagnostic d'adénomyose a été porté pour cinq cas et six contrôles sur l'imagerie. La majorité des patientes avaient de « multiples » fibromes à l'imagerie, traduit par plus de

3. Aucune évaluation de volume du principal fibrome n'a été réalisée par les radiologues. Les calculs de volume utérin étaient différents entre les groupes alors que l'estimation par le radiologue ne l'était pas (p<0,01 vs p=0,07). La répartition du nombre de fibrome était différente entre les groupes (p<0,01). Les autres caractéristiques d'imagerie étaient similaires entres les cas et les témoins. (Tableau 5)

- La procédure d'embolisation

L'EAU était unilatéral par ponction de l'artère fémorale droite dès que possible. En cas d'échec, un abord par l'artère fémorale gauche était réalisé (2,8%). Deux protocoles ont été retrouvés :

-Embosphere® particules de 500-700µm, 700-900µm et 900-1200µm,

-Embozene® (ou Celo Nova) particules de 700µm, 900µm et 1100µm.

Des variantes ajoutaient des particules Embogold®. Une seule fois le Curaspon® n'a pas été ajouté pour terminer la procédure. (Tableau 6) Des micro-cathéters ont été nécessaires (n=7/69, 10,1% des cas et n=21/138, 15,2% dans le groupe contrôle). Dans le groupe contrôle, deux hystéroscopies opératoires ont été réalisées (n=2/21, 9,5%) et deux DIU retirés (n=2/21, 9,5%) concomitamment à l'EAU.

- Analyse univariée

Parmi les facteurs de risque potentiels étudiés, l'immunodépression, l'association DIU et adénomyose, le nombre de fibromes, la localisation sous-muqueuse, le volume estimé du principal fibrome, le volume calculé de l'utérus, le type et la quantité de particules utilisées pour l'embolisation étaient associés de manière significative aux complications en analyse univariée (p<0,05). (Tableau 7)

- Analyse multivariée

Les facteurs de risques significatifs en analyse univariée ont été considérés pour l'analyse multivariée sauf l'immunosuppression et l'association DIU adénomyose dus à leur faible prévalence (n<10). (Tableau 8) Après considération des facteurs de confusion, seule la présence de fibrome sous-muqueux (OR=4,84, IC95%=[1,95; 12,03], p<0,01) était liée aux complications des embolisations des artères utérines. Les formules de Shiota et Harb étaient statistiquement équivalentes et corrélées pour l'évaluation du volume utérin.

4. Prévalence de l'embolisation des artères utérines

Grace au système de codage, 1257 EAU ont été retrouvées sur 15 ans. 85 embolisations ont été réalisées pour une étiologie autre que des fibromes. Au total, 1172 EAU ont été

réalisées pour des fibromes symptomatiques sur 15 ans. Avec 73 cas, notre centre montre un taux global de complications de 6,23% et un taux d'échec de traitement de 3% (n=35/1172).

5. Analyse des perdus de vue

Seulement 28 patientes n'ont pas réalisé d'IRM de contrôle prévu entre 5 et 10 mois post-embolisation et ont été considérées perdues de vue. Le taux de perdus de vue était donc de 2,4%.

## DISCUSSION

1. Principaux résultats :

En analyse multivariée, seul la localisation sous-muqueuse d'au moins un fibrome était associés aux complications post-embolisation des artères utérines ($p<0,01$). L'immunodépression ou l'association DIU adénomyose n'ont pas pu être étudié du fait de leur trop faible prévalence. La présence isolée d'un DIU au moment de l'embolisation n'a pas été retrouvée comme facteur de risque.

2. Comparaison des résultats avec la littérature

Les revues de la littérature et études randomisées contrôlées rapportent un taux de complications de 5 à 8%. (21) (22) (23) La cause principale des hospitalisations est la douleur. (24) (25) La douleur est la conséquence physiologique de l'ischémie induite par l'embolisation. (26) Nous retrouvons un taux similaire de complications dans notre étude. La considération de l'expulsion de fibromes en tant que complication peut être débattue, car correspondant à la finalisation du traitement. (27) (28) (29) Par contre, l'expulsion de fibrome peut se compliquer ou nécessiter un traitement chirurgical, voire engendrer des séquelles. (30) (31) (10) Le traitement des complications est l'hystérectomie dans 1 à 2% des cas. (32) (33) La principale complication retrouvée dans la littérature est l'expulsion de fibrome. (34) (13)

La dernière méta-analyse rapporte un taux de réintervention de 14%, ce qui est très éloigné de notre population. (35)

Pour de nombreux facteurs de risques potentiels, les analyses rétrospectives sont en contradiction avec des études cas témoins ou méta-analyses plus récentes.

Des cas cliniques rapportent des complications suite à des gestes endo-utérins réalisés après EAU. (36) Les études rétrospectives ne peuvent pas conclure sur l'implication du caractère sous-muqueux des fibromes, du type ou quantité de particules en tant que

facteur de risque de complications. (37) De même pour les DIU, qui ne sont pas contre-indiqués pour réaliser une EAU et donc non retirés préventivement. (38) L'IMC et le volume du principal fibrome pourraient être associés aux complications. (14)

Les fibromes sous-muqueux seraient plus à risque d'expulsion. (34) Tout comme la taille des fibromes, leur caractère pédiculé serait un facteur de risque d'expulsion. (39) (13) Ces fibromes seraient moins ischémiés par l'embolisation, ce qui augmente le risque d'échec du traitement. (32) (40) (41) Ces fibromes seraient donc plus à risque de complications, notamment d'échec de traitement. (13) (42)

Les études rétrospectives ne retrouvent pas de corrélation entre volume des fibromes supérieur à 10cm de diamètre et complications. (43) (44) Les fibromes géants (>10cm de diamètre) pourrait quand même être un facteur de risque de complication, tout comme les méga-utérus (>700cc ou >1000cc). (14) (45) Ces méga-utérus pourraient avoir un taux de complications sévères de 20%. (46) Une analyse multivariée ne retrouvait pas de corrélation entre localisation ou nombre des fibromes et complications. (47)

L'essai EMMY montre une relation dose-effet entre la quantité de particules utilisées lors de l'EAU et les complications sévères. (48) Mais une autre étude prospective ne retrouve pas d'association entre la quantité de particules et le risque d'infection. (44)

3. Forces

La principale force de notre étude est son originalité. Comme discuté précédemment, il n'existe que peu d'études sur les facteurs de risques de complications des EAU dans la littérature. Une étude cas-témoins est l'étude la plus adaptée pour répondre à cette question, sachant que ces complications sont rares. Par ailleurs, notre étude démontre la faiblesse des études rétrospectives qui ne peuvent être exhaustives. Notre recherche de prévalence et étude des perdus de vus essaye de réduire la perte de données engendrée par une étude rétrospective.

4. Limites

Une étude rétrospective inclus toujours une perte de données, notamment sur l'évaluation radiologique du volume utérin et du principal fibrome engendrant des limites statistiques. L'ethnie serait un facteur de risque potentiel de complication. (49) Ce critère n'a pu être collecté dans notre étude.

Etudiant une complication rare, l'utilisation d'un critère de jugement composite permet de maximiser le nombre de cas considérés. Mais en parallèle, ce critère de jugement

composite diminue la spécificité des critères analysés. Il se peut que les différentes complications étudiées aient chacune différents facteurs de risques, qui ne seront alors pas identifiables.

Une autre limite de notre étude pourrait être son caractère unicentrique. Cependant, ceci permet l'uniformisation et la reproductibilité des techniques et procédures.

5. Ouverture

Les recommandations internationales divergent principalement sur le rôle de la localisation des fibromes en tant que facteur de risque (sous-muqueux, pédiculé). (15) D'autres facteurs de risques potentiels restent controversés. Notre étude pourrait être incluse dans une future méta-analyse pour statuer sur le risque que représentent les fibromes sous-muqueux. Identifier et connaître ces facteurs de risque pourrait aider les praticiens à guider et conseiller leurs patientes sur la thérapeutique la mieux adaptée à chacune d'elles en considérant leurs facteurs de risque individuels pour éviter une chirurgie en urgence, comme le dit le collège canadien des gynécologues (SOGC). (14) (50) Ils vont même jusqu'à contre indiquer l'embolisation pour les patientes refusant toute hystérectomie. (50) Soit dit en passant, les patientes décrivent avoir une meilleure qualité de vie à 2 ans après un traitement chirurgical qu'une embolisation. (51)

Les recommandations concernant le traitement des fibromes symptomatiques avec ménorragies sont en cours de rédaction ; cette occasion permettrait de nous aligner sur les autres recommandations internationales qui placent l'embolisation en alternative à la chirurgie.

## Abstract

INTRODUCTION Uterine artery embolization (UAE) for symptomatic fibroids is known as a safe treatment course. Complications are rare; but failure of treatment occurs for approximately 13-24% of patients. Potential risk factors of complications are not yet clear in literature.

METHODS We conducted a matched case control study over 15 years in our specialized unit. All Grade 2 complications (or worse) for the Society of Interventional Radiology Standards of Practice Committee were considered, corresponding to severe complications or complications implying a hospitalization.

RESULTS In the 73 included cases' 24,7% hospitalized for pain (n=18/73), 26% for infection (n=19/73) and 2,7% expulsed their fibroid (n=2/73). Overall 35 patients underwent a second procedure (47,9%), most frequently based on surgery (n=18/35, 51,4%). Univariate analysis (n=69) isolated immunosuppression (p=0,02), the association intra-uterine device to adenomyosis (p=0,04), estimated volume of major fibroid (p=0,04), a submucosal localization of fibroid (p<0,01), calculated volume of uterus (p<0,01), type and quantity of used particles (p=0,03) as potential risk factors. Only a submucosal localization of fibroid (OR=4,84, IC95%=[1,95; 12,03], p<0,01) was independently related to UAE's complications.

CONCLUSION Risk factors of UAE complications found was presence of a submucosal fibroid (p<0,01). In that case, women should be informed of the potential adverse events, survey should be programmed and counsel about the other possible treatment plan provided.

# Introduction

Approximately one third of the feminine population suffers from uterine fibroids. (1) Uterine artery embolization is now a well-established conservative treatment for symptomatic fibroids. According to French guidelines, UAE is a good alternative treatment in women with unique myoma of less than 10cm and multiple myomas with a cumulative size of 15cm. (2) (3)

This treatment is well accepted, available in most countries and shows very few complications. (4) (5) It's most frequent complication is a failure of treatment needing a second embolization or a surgical procedure. (6) (7) (8) But some complications can be vital, especially infection. (9) (10)

These complications are rare. (11) Only few case reports are found in literature. (12) Retrospective studies suggest size or localization of fibroids to be linked to complications. (13) Recently, a case control study found uterine volume and BMI to be infective risk factors. (14) Risk factors for adverse event are not yet clear; neither researched due to the limited incidence of uterine artery embolization complications. But we can question their existence. If they do exist, acknowledging them could prevent surgical intervention performed in emergency in order to treat patients affected by an adverse event. So, are there some risk factors we need to acknowledge to preferentially discuss a firsthand surgical treatment with our patients?

In parallel, a recent study points to international guidelines discordances and emphasizes the need to reflect on the objectivity of our guidelines. (15)

In regard of this context, we aim to determine risk factors of uterine artery embolization for fibroids' complications by recalling on patients' treatment course in our specialized unit in a case control study.

# Methods

1- Design

We conducted a retrospective case control study, in the University Hospital of Tours aiming to evaluate risk factors of uterine artery embolization (UAE). All patients who underwent a uterine artery embolization for symptomatic fibroids between January 2005 and June First 2020 were eligible to participate.

Our center performs around 85 embolizations each year with an estimated complication ratio of 5%. Thus, we chose ahead to reflect over the last 15 years to reach around 75 considered patients to be included in our study. Moreover, over the last 15 years, UAE procedures were standardized and electronically documented charts were generalized.

2- Inclusion criteria

a. Cases

Patients presenting at least one severe complication of UAE were included. The complications were considered for the patient's time of follow up in our hospital, whichever the specialist who diagnosed the complication (gynecologist, radiologist, emergencies).

b. Controls

For each case, two controls were selected. All controls were matching cases on department of living, age and year of procedure. Department of habitation was considered Indre-et-Loire department (37) or outside this department. Patient's age at moment of the procedure was referred to as a categorical variable, matching was done within a 2 years range. Year of the procedure was matched within a 2 years range (1 year before and 1 year after the date of case's uterine artery embolization). If several controls were corresponding to a single case, the closest control in age, date of procedure and place of living was selected.

3- Exclusion criteria

Exclusion criterion included pre-operative embolization. Uterine artery embolizations for another cause than fibroids, such as endometriosis, arteriovenous malformation or adenomyosis, were excluded. Associated ovarian artery embolization was accepted. In case of concomitant carcinoma or suspected carcinoma, patients were excluded.

Patients presenting with a vascular complication of uterine artery embolization were not considered. The same rule was applied for minor embolization complication or any hospitalization not related to uterine artery embolization.

4- Data collection

a. Patients

Patients' collection was performed with the help of the Service d'Information Médicale, Epidémiologie et Economie de la Santé (SIMEES) of our study hospital to find the best method enabling us to minimize loss of information. They suggested a key word research within the patients' electronical charts. Choice was made to go back in years as far as electronical charts did exist. Therefore, patients' charts were searched using key words corresponding to the treatment and complications on all patients hospitalized or consulting in gynecology starting in 2005.

In parallel, the CCAM and CIM-10 encoding systems were searched to find patients who underwent an embolization and presented with the complications previously quoted. Both lists were pooled to find as many patients as possible going as far as coding systems could.

However, we do not wanted to miss cases. Therefore a new searching method was put into use. With the help of an epidemiologist, an encoded IT chart was run to perform a chain search in order to find all patients' consultation or hospitalization in gynecology, emergency, internal medicine, infectiology, intensive care unit or reanimation units within 3 months after undergoing UAE in the neuro-interventional unit.

Finally, while performing our loss to follow up research, 16 more potential cases were identified. Of the 16 patients, 9 additional cases were included in the study.

For patients undergoing several uterine embolization procedures, the earliest UAE performed in our hospital ward was considered.

b. Follow-up

Uterine artery embolizations are performed in the neuro-vascular specialized unit. Afterwards, all patients are hospitalized overnight in the gynecological ward. When leaving the hospital, prescriptions include level 2 analgesia and anti-inflammatory medication for a couple of weeks.

All patients had a follow-up MRI programmed around 6 to 8 month after the date of UAE. Being a specialized referent unit, a third of the patients come from other departments in the country. Thus patients living in other departments were still followed in our teaching hospital.

c. Complications

Only severe complications or complications implying a hospitalization were considered following the Society of Interventional Radiology Standards of Practice Committee (SIR). (16) Early complications were defined as occurring in the first three months after uterine artery embolization, and later complications were defined by a diagnostic three months past UAE and were considered for the time of follow up in our hospital. (52) Thus for early complications, we considered infection or sepsis, expulsion, vaginal bleeding, pain and emergency surgery as complications. Pain was included if it needed hospitalization for intra-venous analgesia or step 3 analgesic. In the same way, infection was considered if bacterial cultures were positive, need for intra-venous antibiotic treatment or hospitalization of the patient. All clinically diagnosed fibroid expulsions were considered. Expulsion diagnosed on imaging reevaluation was not considered. Patients presenting with vaginal bleeding who consulted in emergency were considered as cases.

Failure of the procedure defined by necessity of a second embolization or a surgical procedure was also registered as a complication. Patients complaining of pollakiuria, minimal vaginal bleeding or pelvic heaviness had an indication of a second treatment. These symptoms were not considered as severe symptomatic complications.

Post-embolization syndrome is defined by pain and/or low-grade fever, sometimes associated to nausea and vomiting, appearing within 72 hours after UAE and resolved within 10 days. Post-embolization syndrome was not considered as a complication unless hospitalization was required to administer IV analgesia.

d. Risk factors

All potential risk factors found in literature were considered: BMI, active smoking, presence of intra-uterine device, sub-mucosal fibroids, volume of uterus and of the larger fibroid, volume of particles injected, model of particles injected, associated treatment or known infection at time of embolization. The combination of intra-uterine device (IUD) with adenomyosis was also focused on as a potential infection risk factor.

Pelvic MRI was performed to assess presence and number of fibroids, measure uterine and/or fibroid volume and to classify fibroids using FIGO classification. PACS imaging software was used for all patients. Volume of uterus was registered from imaging report by a radiologist. If only its width, length and depth were registered; uterus volume was calculated using Shiota (Uterine volume= (length x width x height x 0,35) + 107) and Harb methods (Uterine volume=length x height x width x 0,52). (17) (18) A second blinded review of all pelvic imaging was asked to another team of radiologist to assess uterine and major fibroids volume.

Equally, if the imaging team did not calculate the volume of the largest fibroid, an ellipsoid formula was applied to its wider measurement to estimate its volume. (19) Patient was considered having submucosal risk factor if at least one of her fibroids were described as sub-mucosal by the radiologist.

Concerning embolization procedure, all aspects were collected using operative reports.

5- Statistics

All statistics and plan was beforehand advised and approved by our teaching hospital statistics and epidemiological department.

a. Statistical plan

To be as thorough as possible, we aimed to achieve three goals:

1. Case control study to analyze potential risk factors
2. Collect the number of uterine artery embolization performed in our specialized center over the 15 years period in order to estimate the complication rate
3. Estimate number of patients lost to follow up

b. Analysis

Qualitative variables were described by frequency and rate. Outcomes of quantitative variables were compared by Chi square method or Fischer's exact test if number of patients was inferior to five in any category. Quantitative variables were described by mean and were compared using a Z method or Student t test.

Univariate analysis was performed by linear correlation analysis. Binary logistic regression analysis included only the variables with a significant threshold of $p<0,20$. Independent variables presenting with an incidence of ten or less were excluded from the multivariate analysis. (20) Univariate and multivariate regression analysis were performed using the SPSS statistics software (version 20, IBM).

The $\alpha$ risk considered was of 5% for bilateral testing.

c. Retrospective study

CCAM act encoding system was used to collect the overall number of uterine artery embolization performed in our center. A cross matching study with diagnostic coding system for fibroids was done to distinguish specifically uterine artery embolization performed to cure symptomatic fibroids.

To estimate lost to follow up, all MRI performed 5 to 10 month after UAE were collected via CCAM encoding system. The CCAM was cross-matched with CIM-10 diagnostic system to individualize MRI performed to evaluate fibroids after UAE within a 5 to 10 months range, overlapping the 6 to 8 months period within which patients are automatically programed to have an evaluation MRI. If missing, patient was considered lost to follow up.

6- CNIL

In regard of ethical considerations and patient's information, the Commission Nationale de l'Informatique et des Libertés (CNIL) approved our study and data collection. No further ethical approval was needed for a retrospective study on charts.

# Results

1- Prevalence of uterine artery embolization

Referring to CCAM coding system we collected a total of 1257 uterine artery embolization procedures performed over the 15 years period. 85 were performed for another etiology than fibroids. In total, 1172 uterine artery embolizations were performed in our center in 15 years to cure uterine fibroids.

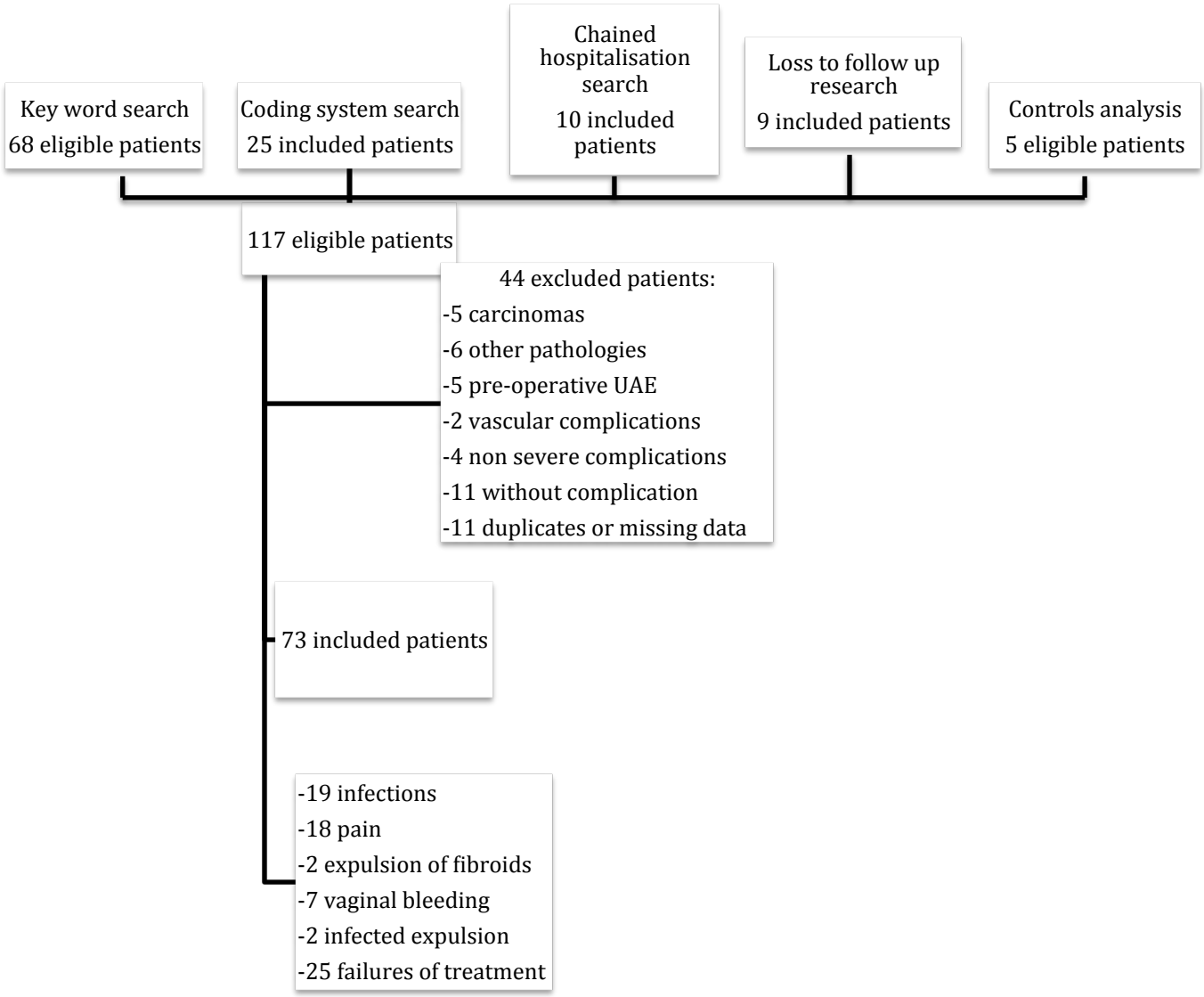
2- Cases collection

Sixty-eight cases were found using the patient's chart research by key words. After researching our center CCAM and CIM-10 encoding system, 14 patients were already eligible, 343 patients were excluded and twenty-five new patients were included in the study. A final group of ten patients were found by an epidemiologist specific research. A total of 103 patients were therefore eligible to participate in our study. Out of the 103 patients, 43 were excluded.

The exclusion criteria were: five carcinoma or suspected carcinoma, six pathology other than fibroids, 5 pre-operative embolization, 2 vascular complications, 4 non severe complications, 11 without any complications, 6 missing imaging report and 4 with no electronical chart.

Performing the lost to follow up researched, an additional 9 patients were found and included. And a final 5 more eligible patients were discovered by analyzing controls to match the first 69 patients and 4 were included because one was a duplicate. In the end, 73 patients were included in our study. (Figure 1)

**Figure 1: Flow chart**




3- Descriptive results

a. Cases' population

A total of 73 cases between 26 and 54 years old were included in our study. Four of them presented with immunosuppression: one had rheumatoid polyarthritis, a second one a polyclonal hypergammaglobulinemia and the last two had HIV under treatment. Fourteen had a long history of fibroids with anterior surgical treatment; one underwent high-intensity focused ultrasound ablation of fibroid therapy (HIFU). (Table 1)

**Table 1: Initial characteristics of cases.**

| General History | Cases (n=73) |
|---|---|
| **Mean age (years)** | 40,8 +/- 6,2 |
| **(m+/- SD)** | (26-54) |
| **Mean BMI (kg/m²)** | 25,1 +/-13,2 |
| **(m+/- SD)** | (19-44) |
| **Active smoking (n,%)** | 5 (6,8%) |
| **Delay before treatment (years)** | 3,1 +/- 2,2 |
| **(m+/- SD)** | (0-12) |
| **Immunosupression (n,%)** | 4 (5,5%) |
| **Obstetrical history** | |
| **Nulliparous (n,%)** | 17 (23,3%) |
| **Mean parity (n,%)** | 1,56 +/- 1,2 (0-5) |
| **Perimenopause (n,%)** | 2 (2,8%) |
| **Menopause (n,%)** | 0 |
| **Gynecological history** | |
| **Adenomyosis (n,%)** | 1 (1,4%) |
| **Endometriosis (n,%)** | 2 (2,7%) |
| **History of myomectomy (n,%)** | 13 (17,8%) |
| • Laparotomy (n,%) | 6 (8,2%) |
| • Hysteroscopy (n,%) | 7 (9,6%) |
| **History of HIFU (n,%)** | 1 (1,4%) |
| **History of uterine evacuation (n,%)** | 11 (15,1%) |

*HIFU: High Intensity Focalized Ultrasounds, m: mean, SD: standard deviation*

Twenty-one cases were not taking any medication at inclusion: no contraception, no analgesia, anti-fibrinolytics or iron supplementation was reported in their charts. Four patients were taking chronic medication for pathologies without relation to fibroids (one L-thyroxin supplementation, one anti- high blood pressure treatment, two tritherapy). In the "other treatment" group, five patients were self-medicating themselves with anti-inflammatory drugs as pain killers. (Table 2)

**Table 2: History of medical treatment of cases.**

| Treatment of patients (n,%) | Cases (n=73) |
|---|---|
| **Intra-uterine device** | 15 (20,5%) |
| **Contraceptive pill** | 22 (30,1%) |
| **Chlormadinone or Normegestrol** | 14 (19,2%) |
| **Ulipristal - Esmya®** | 2 (2,7%) |
| **LHRH analogs** | 1 (1,4%) |
| **Iron supplements** | 9 (12,3%) |
| **Anti-fibrinolytic** | 15 (20,5%) |
| **Transfusion** | 3 (4,1%) |
| **Other treatment** | 7 (9,6%) |

b. Complications

i. Overall complications

The overall main complication presented by cases was mostly pain (n=18/73, 24,7%) and infection (n=19/73, 26%) including sepsis (n=7/73, 9,6%). Isolated asymptomatic failure of treatment represented 34,2% (n=25/73) of complications. (Figure 2)

Many patients presented with painful infection or vaginal bleeding and pain associated to fibroid expulsion. This situation is different from consecutive complications occurring on different emergency consultation or hospitalization. In the overall population of 73 cases, 24 presented with several symptoms considered as complications (n=24/73, 32,9%) and 41 presented with several complications (including failure of treatment, n=41/73, 56,2%). 14 had consecutive complications needing several consultation or hospitalization (n=14/73, 23,3%).

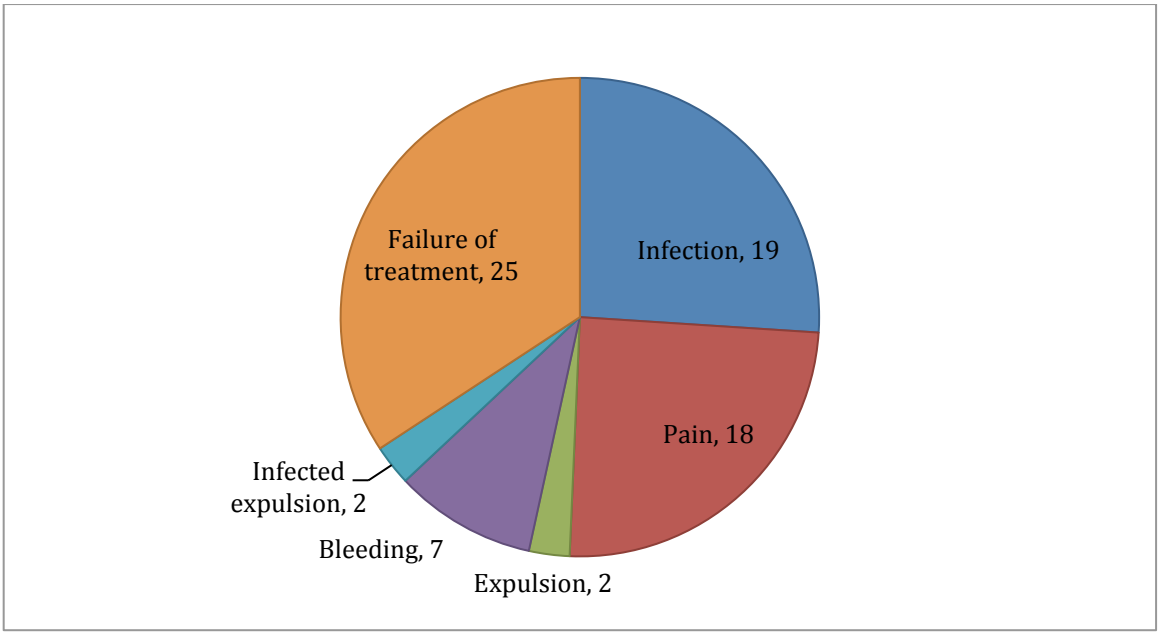
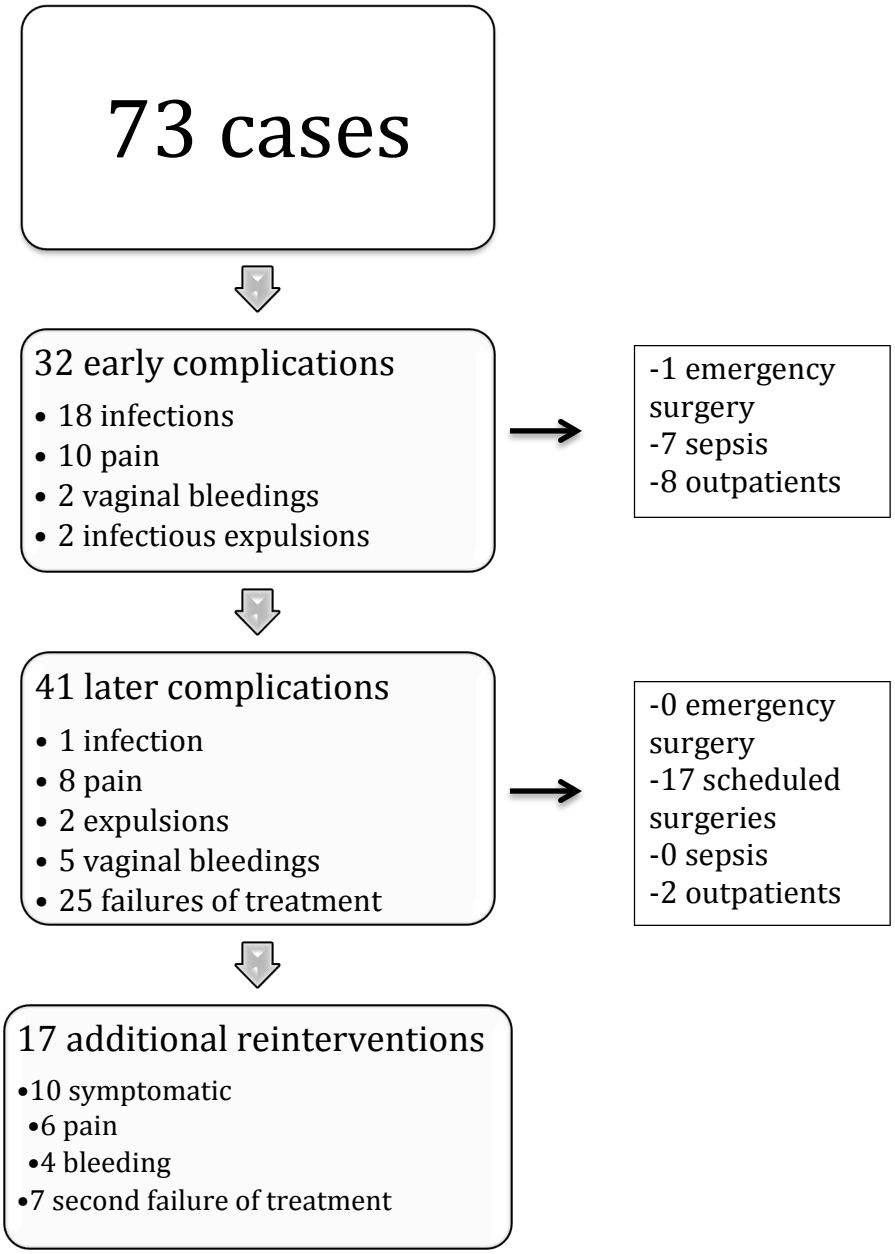



**Figure 2: Distribution of first complication presented by cases.**

**Figure 3: Flow chart of complications presented by cases.**




ii. Early complications

Thirty-two cases (n=32/73, 43,8%) were hospitalized within the first three months showing, by definition, early complications. The early complications were infection (n=18/32, 56,3%), including sepsis (n=7/32, 21,9%), 2 infected fibroid expulsion (n=2/32, 6,3%), pain needing intra-venous or opioid analgesic treatment (n=10/32, 31,3%) and vaginal bleeding (n=2/32, 6,3%). Fibroid expulsion happened once in a second time, with necessity of a second hospitalization for pain (n=1/32, 5,8%). One patient underwent emergency surgery (n=1/32, 5,8%).

Eight patients with complications were not hospitalized of whom 3 patients presented with infection with confirmed bacterial infection on vaginal swab treated by oral antibiotics (n=3/73, 4,1%), one presented with vaginal bleeding (n=1/73, 1,4%), 1 with pain needing step-3 analgesia (n=1/73, 1,4%), two with fibroid expulsion (n=2/73, 2,7%) and one with infected expulsion of fibroid (n=1/73, 1,4%).

iii. Later complications

Later complications were defined as occurring at least 3 months after uterine artery embolization. Forty-one cases (n=41/73, 56,2%) presented later complications. The late complications reported were: infection (n=1/41, 2,4%), but no sepsis, pain (n=8/41, 19,5%), fibroid expulsion (n=2/41, 4,9%), and vaginal bleeding (n=5/41, 12,2%). Failure of treatment was the major cause of patients' return to the hospital (n=25/41, 61%). (Figure 3 and 4) Almost all patients were hospitalized (n=39/41, 95,1%). The two patients not needing to be hospitalized presented with aseptic necrobiosis and fibroid expulsion.

We report 6 asymptomatic expulsion of fibroids discovered on MRI performed during follow-up in the control group (n=6/73, 8,2%).

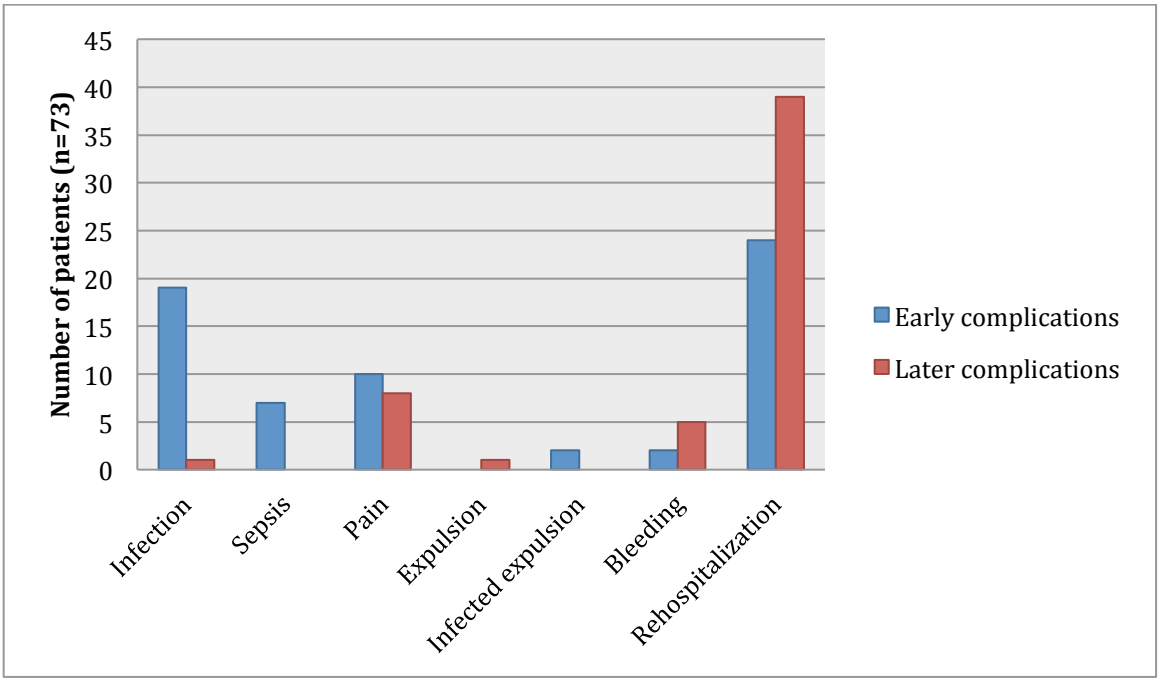
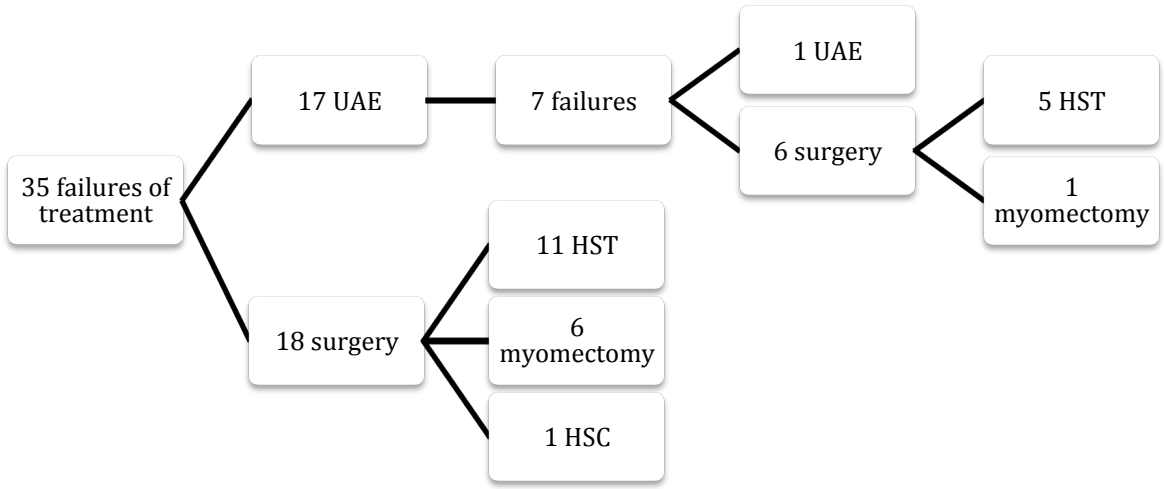



**Figure 4: Distribution of early and later complications presented by cases.**

Overall 35 patients (n= 35/73, 47,9%) were not clinically improved by the embolization and required a second course of treatment, which consisted on a second uterine artery embolization (n=19/35, 54,3%) or surgery (n=16/35, 45,7%). Surgical course consisted on myomectomy (n=6/16, 37,5%), hysterectomy (n=9/16, 56,3%) or fibroid resection by hysteroscopy (n=1/16, 6,3%). Mean delay of overall second treatment was 3,1 years +/- 2,5 (4,5 months-8,6 years). Seven patients underwent a third treatment course (n=7/35, 20%) of which one underwent a third UAE (n=1/7, 14,3%) and six underwent surgery (n=6/7, 85,7%). (Figure 3 and 5)

**Figure 5: Treatments performed in case of failure of uterine artery embolization.**




*HSC: hysteroscopy, HST: hysterectomy, UAE: uterine artery embolization.*

25 patients (71,4%) were non-symptomatic or had non-severe symptoms leading to a second course of treatment; and 10 patients (28,6%) did present a previous symptomatic complication before undergoing a reintervention.

Ten cases presented a symptomatic failure of treatment (n=10/35, 28,6%). Two presented with combined pain and vaginal bleeding (n=2/10, 20%); six with only pain (n=6/10, 60%), the other two with isolated vaginal bleeding (n=2/10, 20%). Semi

emergency second course of treatment consisted of a second embolization (n=3/10, 30%) or emergency surgical procedure (n=7/10, 70%). For symptomatic patients, treatment was mostly surgical balanced between hysterectomies (n=3/10, 30%) and myomectomies (n=3/10, 30%). Fewer hysteroscopic resections of fibroid (n=1/10, 10%) were performed. (Figure 6) For symptomatic patients, mean delay of second course of treatment was 2,1 years +/- 2,1 (4,5 months-7,3 years).

We quantified 25 patients (71,4%) presenting with non- severe symptomatic failure of treatment, who consulted to undergo a second treatment course. 64% of asymptomatic patient were willing to undergo a second UAE (n=16/25). Mean delay of second treatment was 3,5 years +/- 2,6 (4,5 months-8,6 years) for asymptomatic patients.

With 73 cases patients, our center had an overall complication rate of 6,23% (n=73/1172) and a 3% failure of treatment rate (n=35/1172).

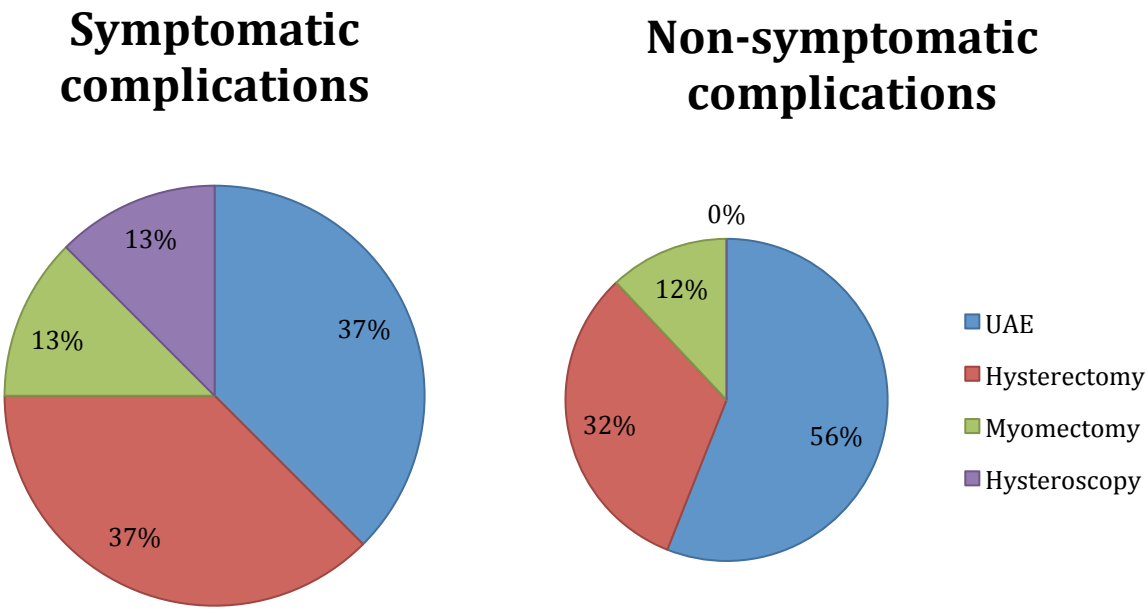



**Figure 6: Choice of treatment course of symptomatic vs non-symptomatic patients or presenting with repeated complications (n=35).**

Pooling all reinterventions, patients were more inclined to undergo surgery (17 UAE vs 18 surgeries); even more so for symptomatic patients, surgical treatment was the preeminent choice (n=9/10 for symptomatic patients vs n=11/25 for non symptomatic patients). (Figure 6)

c. Case control study population

Four cases did not have two corresponding controls. Enlarging controls stratification criteria to 3 years for age range or year range of uterine artery procedure did not permit to find controls for these patients. Thus, they were not included in the case control study.

One was the most morbidly obese of the cases (BMI=43,5kg/$m^2$) presenting with a single fibroid of 55mm who was hospitalized immediately of discharge needing IV analgesia. Two cases without controls had a moderate increased uterine volume (150-180cc) due to a single fibroid with a failure of treatment. They both underwent a second UAE after a long delay being asymptomatic. The last one had multiple fibroids in her uterus around 5cm diameter each for the major ones resolving in a failure of treatment. This patient underwent myomectomy several years later.

4- Case control analysis on risk factors

a. Characteristics of the case control population

The control population did not include immunosuppression; therefore immunosuppressed patients were more in the cases group (p=0,02). However, the control group showed more comorbidities and chronic diseases than the cases group, therefore using more long-term medication (p<0,01) The most frequent were: 9 high-blood pressure, 4 diabetes, 7 hypothyroidisms and 5 depressions.

The population was similar on the other clinical criteria studied (Table 3) and medication (Table 4).

**Table 3: Initial characteristics of the case control study population.**

| General History | Cases (n=69) | Controls (n=138) | p |
|---|---|---|---|
| **Mean age (years)** | 40,8 +/- 6,3 | 41,6 +/- 5,9 | |
| **(m+/- SD)** | (26 - 54) | (26 - 53) | 0,43 |
| **Mean BMI (kg/m²)** | 24,7 +/-4,5 | 27,2 +/-7,6 | |
| **(m+/- SD)** | (19 - 37) | (18 - 50) | 0,07 |
| **Active smoking (n,%)** | 5 (8,3%) | 11 (12%) | 0,48 |
| **Delay before treatment (years)** | 3,1 +/- 3,2 | 4,7 +/- 5,2 | 0,22 |
| **(m+/- SD)** | (0 - 12) | (0 - 20) | |
| **Immunosuppression (n,%)** | 4 (5,9%) | 0 | *0,02* |
| **Obstetrical history** | | | |
| **Nulliparous (n,%)** | 16 (24,6%) | 30 (25,4%) | 0,91 |
| **Mean parity (n,%)** | 1,54 +/- 1,2 (0-5) | 1,56 +/- 1,4 (0-8) | 0,92 |
| **Perimenopause (n,%)** | 2 (2,9%) | 7 (5,6%) | 0,40 |
| **Menopause (n,%)** | 0 | 0 | *NA* |
| **Gynecological history** | | | |
| **Adenomyosis (n,%)** | 1 (1,4%) | 3 (2,5%) | 0,54 |
| **Endometriosis (n,%)** | 1 (1,4%) | 4 (3,3%) | 0,66 |
| **History UAE (n,%)** | 1 (1,4%) | 1 (0,8%) | 0,59 |
| **History of myomectomy (n,%)** | 13 (18,8%) | 23 (18,5%) | 0,96 |
| • Laparotomy (n,%) | 6 (8,7%) | 12 (9,8%) | 0,81 |
| • Hysteroscopy (n,%) | 7 (10,1%) | 11 (8,9%) | 0,78 |
| **History of HIFU (n,%)** | 1 (1,4%) | 2 (1,6%) | 0,71 |
| **History of uterine evacuation** | 11 (17,2%) | 9 (8%) | 0,06 |

*HIFU: High Intensity Focalized Ultra-sound, UAE: uterine artery embolization.*

**Table 4: History of medical treatment of the case control study population.**

| Treatment of patients (n,%) | Cases (n=69) | Controls (n=138) | p |
|---|---|---|---|
| **Intra-uterine device** | 15 (23,1%) | 23 (21,3%) | 0,78 |
| **Contraceptive pill** | 22 (34,9%) | 50 (46,3%) | 0,15 |
| **Chlormadinone or Normegestrol** | 14 (20,9%) | 29 (27,1%) | 0,36 |
| **Ulipristal - Esmya®** | 2 (3%) | 11 (10,1%) | 0,14 |
| **LHRH analogs** | 1 (1,5%) | 6 (5,5%) | 0,25 |
| **Iron supplements** | 9 (13,2%) | 14 (13%) | 0,96 |
| **Anti-fibrinolytic** | 15 (22,1%) | 17 (15,7%) | 0,29 |
| **Transfusion** | 3 (4,4%) | 1 (0,9%) | 0,30 |
| **Other treatment** | 7 (10,8%) | 33 (30,3%) | *<0,01* |

b. MRI characteristics

For 5 cases and 6 controls adenomyosis was diagnosed on the MRI performed to evaluate fibroids.

The majority of the population had "multiple" fibroids described in the imaging report. Referring to the MRI, "multiple fibroids" was described over 3 fibroids by the radiologist. No report included major fibroid volume evaluation but fibroids measurements instead. Fibroid volume approximation by an ellipsoid formula was the only volume approximation available for all of the patients.

Uterine volume calculated by Shiota et al. or Harb et al's methods were significantly different between groups compared to radiologist uterine volume estimation (p=0,07 and p<0,01 for mathematical formulas). Number of fibroids and volume of major fibroid differed from groups (p<0,01). Other imaging characteristics were similar between groups (Table 5).

**Table 5: Initial imaging characteristics of the case control study population.**

| Imaging characteristics | Cases (n=69) | Controls (n=138) | p |
|---|---|---|---|
| **Adenomyosis** | 6 (8,7%) | 9 (6,5%) | 0,55 |
| **Endometriosis** | 2 (3,3%) | 5 (3,6%) | 0,58 |
| **Presence of IUD** | 12 (17,4%) | 13 (9,4%) | 0,11 |
| **Mean uterine volume (mL)** | | | |
| • Described (n =18) | 1010,4+/-999,2 (293 - 3426) | 357,3+/- 171,8 (115 - 664) | 0,07 |
| • Shiota (n =127) | 451,6 +/- 430,8 (30 - 2293) | 277,2 +/- 181,4 (52 - 824) | *<0,01* |
| • Harb (n =127) | 670,7 +/- 640,0 (44 - 3407) | 411,7 +/- 269,6 (77 - 1225) | *<0,01* |
| **Number of fibroids** | | | |
| • 1 | 19 (27,5%) | 41 (29,7%) | *<0,01* |
| • 2 | 10 (14,5%) | 18 (13%) | |
| • 3 | 7 (10,1%) | 7 (5,1%) | |
| • >3 | 26 (37,7%) | 71 (51,4%) | |
| • Unknown | 7 (10,1%) | 1 (0,7%) | |
| **Volume of major fibroid (mL)** | | | |
| • Described | NA | NA | *NA* |
| • Ellipsoid volume (n = 193) | 35,9 +/- 14,7 (5 - 99) | 31,5 +/- 12,9 (5 - 79) | *0,04* |

*IUD: intra-uterine device.*

c. Embolization characteristics

Uterine artery embolization is done routinely in our center. Sixty-six cases underwent UAE with the same operator, whether the last three had a second operator. Uterine artery embolization was unilateral by puncture of the right femoral artery. Only if the right femoral artery was not usable, the left femoral artery was punctured. Twice was the right femoral artery not possible to puncture (2,8%).

Two methods were registered:

-Embosphere® particles of size 500-700µm, 700-900µm and 900-1200µm,

-Embozene® (also referred as Celo Nova) particles of size 700µm, 900µm and 1100µm

Variable methods included mixing Embosphere® and Embozene® particles or adding Embogold® particles to Embosphere® particles. Only once did injecting Curaspon® intra-arterially not finish the procedure. (Table 6)

Additional procedures in the cases group included micro-catheters (n=7/69, 10,1%) and two failures of procedure on the right femoral artery being transformed by a left femoral artery catheterization. For controls, additional procedures consisted of two operative hysteroscopy on the same day of the UAE (9,5%), two IUD removals (9,5%) and the rest of need to use micro-catheters to embolize uterine arteries (n=17/21, 81%).

On control MRI performed 5 to 10 month after UAE, 16 cases showed non-devascularized fibroids (26,7%) compared to 6 controls (4,7%, $p<0,01$). Among these patients, 4 presented with infection (n=4/16, 25%), 2 with pain (12,5%) and the others failure of treatment (n=10/16, 62,5%).

**Table 6: Characteristics of embolization procedures.**

| Embolization characteristics | Cases (n=69) | Controls (n=138) | p |
|---|---|---|---|
| **Type of particles** | | | |
| • Embosphere® | 38 (55,1%) | 80 (58%) | *<0,01* |
| • Embozene® | 22 (31,9%) | 56 (40,6%) | |
| • Embosphere®+Embozene® | 5 (7,2%) | 0 | |
| • Embosphere®+Embogold® | 1 (1,4%) | 2 (1,4%) | |
| • Unknown | 3 (4,3%) | 0 | |
| **Mean quantity of particles (number of flask) (m+/- SD)** | 7,9 +/- 4,3 (2-23) | 6,7 +/- 2,8 (1-16) | *0,02* |
| **Mean quantity of Curaspon® (pieces) (m+/- SD)** | 10,3 +/- 3,9 (0-18) | 10,2 +/- 3,4 (2-23) | 0,90 |
| **Site of embolization** | | | |
| • Right femoral artery | 65 (94,2%) | 134 (97,1%) | 0,50 |
| • Left femoral artery | 1 (1,4%) | 1 (0,7%) | |
| • Right and left femoral arteries | 1 (1,4%) | 0 | |
| • Unknown | 2 (2,9%) | 3 (2,2%) | |
| **Operator performing the embolization** | | | |
| • Operator 1 | 66 (95,7%) | 124 (89,9%) | 0,45 |
| • Operator 2 | 3 (4,3%) | 7 (5,1%) | |
| • Operator 3 | 0 | 5 (3,6%) | |
| • Operator 4 | 0 | 1 (0,7%) | |
| • Operator 5 | 0 | 1 (0,7%) | |

*M: mean, SD: standard deviation.*

d. Univariate analysis

Among the risk factors taken into consideration, in univariate analysis immunosuppression, the association of IUD to adenomyosis, estimated volume of major fibroid, presence of a submucosal fibroid, estimated volume of uterine volume, type and quantity of particles are significantly linked to uterine artery complications ($p<0,05$).

Presence of an intra-uterine device is not correlated to UAE complication ($p=0,11$) but the association of adenomyosis and IUD increased the risk of UAE complications ($p=0,04$). Immunosuppression could be a risk factor of UAE complication as well ($p=0,02$).

Results of univariate analysis are shown in Table 7.

The patient showing a concomitant infection was diagnosed with a mycoplasma vaginal infection 10 days prior to UAE.

**Table 7: Univariate analysis of considered risk factors.**

| Risk factors | Cases (n=69) | Controls (n=138) | OR | IC 95% | p |
|---|---|---|---|---|---|
| **Clinical factors** | | | | | |
| • Mean BMI (m+/- SD) | 24,7 +/-4,5 (19-37) | 27,2 +/-7,6 (18-50) | 0,93 | 0,87; 1,01 | 0,07 |
| • Active smoking | 5 (7,2%) | 11 (8%) | 0,67 | 0,22; 2,03 | 0,48 |
| • Immunosuppression | 4 (5,8%) | 0 | NA | NA | *0,02* |
| • Concomitant infection | 1 (1,4%) | 0 | NA | NA | 0,17 |
| **Imaging factors** | | | | | |
| • Intra-uterine device | 12 (17,4%) | 13 (9,4%) | 1,99 | 0,85; 4,66 | 0,11 |
| • Adenomyosis | 6 (8,7%) | 9 (6,5%) | 1,39 | 0,47; 4,09 | 0,55 |
| • Adenomyosis + IUD | 4 (5,8%) | 1 (0,7%) | 0,12 | 0,01; 1,08 | *0,04* |
| • Major fibroid volume (mL) | | | | | |
| ➢ **Measurement** | NA | NA | NA | NA | *NA* |
| ➢ **Ellipsoid approximation** | 35,9 +/- 14,7 | 31,5 +/- 12,9 | 1,02 | 1,00; 1,05 | *0,04* |
| • Submucosal fibroid | 51 (73,9%) | 78 (56,5%) | 3,27 | 1,60; 6,67 | *<0,01* |
| • Number of fibroids | | | | | |
| ➢ **< ou =3** | 36 (52,2%) | 66 (47,8%) | 0,67 | 0,37, 1,23 | 0,20 |
| ➢ **>3** | 26 (37,7%) | 71 (51,4%) | | | |
| ➢ **Unknown** | 7 (10,1%) | 1 (0,7%) | | | |

| | | | | | |
|---|---|---|---|---|---|
| • Uterine volume (mL) | | | | | |
| ➢ **Described** | 1010,4+/-999,2 (293-3426) | 357,3+/-171,8 (115-664) | 1,01 | 0,99; 1,01 | 0,07 |
| ➢ **Shiota** | 451,6 +/- 430,8 (30 - 2293) | 277,2 +/- 181,4 (52 - 824) | 1,00 | 1,00; 1,01 | *<0,01* |
| ➢ **Harb** | 670,7 +/- 640,0 (44 - 3407) | 411,7 +/- 269,( (77 - 1225) | 1,00 | 1,00; 1,00 | *<0,01* |
| **Catheterization factors** | | | | | |
| • Type of particles | | | | | |
| ➢ **Embosphere®** | 38 (55,1%) | 80 (58%) | 6,32 | 1,22; 32,76 | *0,03* |
| ➢ **Embozene®** | 22 (31,9%) | 56 (40,6%) | | | |
| ➢ **Embosphere® + Embozene®** | 5 (7,2%) | 0 | | | |
| ➢ **Embosphere® + Embogold®** | 1 (1,4%) | 2 (1,4%) | | | |
| ➢ **Unknown** | 3 (4,3%) | 0 | | | |
| • Mean quantity of particles | 7,9 +/- 4,3 (2 - 23) | 6,7 +/- 2,8 (1 - 16) | 1,11 | 1,01; 1,21 | *0,03* |
| • Mean quantity of Curaspon® | 10,3 +/- 3,9 (0 – 18) | 10,2 +/- 3,4 (2 – 23) | 1,01 | 0,92; 1,10 | 0,90 |
| • Additional procedure | 9 (13%) | 21 (15,2%) | 0,86 | 0,37; 2,01 | 0,73 |

*IC 95%: interval of confidence 95%, M: mean, OR: odd's ratio, SD: standard deviation*

e. Multivariate analysis

We considered only significant factors in univariate analysis: immunosuppression, BMI, presence of IUD, the association of IUD and adenomyosis, volume of the uterus evaluated by Shiota or Harb's methods, number of fibroids and volume of major fibroid, its submucosal localization, quantity and type of particles. Immunosuppression and the association of IUD to adenomyosis were not included in the multivariate analysis due to insufficient prevalence (n<10). (Table 8)

Shiota et al. or Harb et als' methods to evaluate uterine volume was statistically equivalent. These evaluations of uterine volume suffered many missing datas impacting strongly on multivariate analysis. Any of these were strongly correlated (p=0,99). Thus, it was removed from multivariate analysis.

**Table 8: Multivariate analysis of significant risk factors.**

| Multivariate analysis | OR | IC 95% | p |
|---|---|---|---|
| IUD | 2,10 | 0,87; 5,07 | 0,10 |
| BMI | 0,93 | 0,86; 1,01 | 0,07 |
| Number of fibroids | 0,57 | 0,27; 1,21 | 0,14 |
| Major fibroid volume | 1,01 | 0,98; 1,05 | 0,40 |
| Submucosal fibroid | 4,84 | 1,95; 12,03 | *<0,01* |
| Quantity of particles | 1,05 | 0,91; 1,21 | 0,50 |
| Type of particles | 2,22 | 0,31; 15,98 | 0,25 |

*BMI: body mass index, IC 95%: interval of confidence 95%, IUD: intra-uterine device, OR: odd's ratio*

After considering confounding factor, presence of a submucosal fibroid was (OR=4,84, IC95%=[1,95; 12,03], p<0,01) related to uterine artery embolization complications.

5- Lost to follow-up

Only 28 patients over 1172 did not perform the control MRI planned 5 to 10 months after UAE in our teaching hospital. Therefore were considered them lost to follow up. The rate of lost to follow up was therefore of 2,4% of patients.

# Discussion

1- Main results

Our reference center shows a complication rate of 6,2% and a 3% of failure of treatment (n=73/1172 and n=35/1172 respectively). In multivariate analysis, only presence of a submucosal fibroid (OR=4,84, IC95%=[1,95; 12,03], p<0,01) was related to uterine artery embolization complications.

2- Comparison of our results with literature

A- Early complications

Review of literature and randomized control trials report around 5-8% of complications. (21) (22) (23) The main cause of hospitalizations is pain-related. (24) (25) Pain is a physiological consequence of UAE being the symptom of ischemia. (26) Our complication rate is similar to the ones found in literature, reinforcing the external validation of our study. Also we may question if fibroid expulsion really is an adverse event, ending in complete cure of patients. (53) (27) (28) (29) However, pain or need of an additional treatment during expulsion should be considered as an adverse event; especially if almost half of the patients need surgery to complete or release pain from fibroids expulsion and because expulsion triggers infection and might end up in sequel: necrosis or fistula. (30) (10) (31) Resolution of a complication can result in hysterectomy in up to 1 to 2% of cases. (32) (33)

Meanwhile the main complication reported in literature is fibroid expulsion, treated within the hospital or as outpatients. (34) (13) Focusing on severe complications following the SIR classification our study did not collect minor complications, including pain-free fibroid expulsion. Thus we might have minimized our incidence of fibroid expulsions. This bias could explain that fibroid expulsion was a minor cause of the complications collected in our study compared to its incidence in literature.

Recently, the Society of Interventional Radiology Standards of Practice Committee established a renewed classification of adverse events combining post-operative and imaging complications. (54) In this new classification duration of hospitalization is not reported but treatment course is more detailed. Aside antipyretic drug (considered a

minor complication) our cases respect these new criteria of moderate to severe adverse events.

B- Failure of treatment

Failure of treatment defined by necessity of a second treatment course is the usual endpoint used in recent studies. (55)

According to the 2012 French guidelines, less than 2% hysterectomies are performed within 3 months of UAE for a complication, but 13 to 28% secondary hysterectomies are performed within 5 years for a UAE failure. (3) (2) Globally, literature reports a rate of 15 to 33% within one to two years after UAE. (7) (56) The risk of reintervention increases with time (after 2 years (RR=3.74, 95% CI=[1.76-7.96]; p= 0.0006), after 5 years (RR=5.01, 95% CI= [1.37-18.39]; p= 0.02 or OR around 10 within 5 years). (35) (22) A prospective study records size of the dominant fibroid and number of fibroids to be predictive factors of need of reintervention with each 1 cm increase: HR = 1.68, 95% CI 1.10-2.69, and each additional fibroid: HR = 1.34, 95% CI 1.08-1.66. (52) The latest meta-analysis reports an overall 14% reintervention rate. (35) We might have missed late second treatment, as women not always came from our center or region and could have been operated on in another center after the usual survey in our hospital.

C- Risk factors

For many potential risk factors, numerous retrospective studies are in contradiction with recent case control studies or meta-analysis.

Patients with a history of intra-uterine surgery seem more at risk of adverse events in our study (p=0,06). Case reports present infectious adverse event following intra-uterine act after UAE. (36) Retrospective studies are inconclusive on submucosal fibroid, type of embolic agent, quantity of particles and size or location of dominant fibroid as risk factor of infection. (37) Likewise, they could not resolve if IUD is a risk factor of infectious complication after UAE but conclude that IUD should not be considered a contraindication to perform UAE. (38) But BMI and major fibroid volume could be linked to infectious complications. (14) Our study is in contradiction with Mollier et al.. BMI was smaller in our cases' population. But it was performed on a French population, known to be leaner, and one of the larger women was excluded. Immediate injection of antibiotics did not change the infection rate post-procedure. (57) Infectious

complications most of the time resolved without surgery. As it could damage the uterine cavity for pregnancy, it could be an important risk. Being a rare complication it is difficult to define risk factor for it.

Size of fibroid, localization of fibroids, especially pedonculated submucosal fibroids, could also be risk factor of expulsion. (39) Submucosal small fibroids (<66cc) are more prone to expulsion. (34) While submucosal fibroids of more than 6 cm diameter might be more at risk of complication if not expulsed. (58) Maybe because they are more likely to migrate towards uterine cavity after UAE. (59) These fibroids are associated with an increased risk of complication in univariate analysis (HR=2,28, IC95%=[1,24-4,8] p<0,01). (13) And a prospective study reports a reintervention rate of 35% with an increased risk of reintervention if patient present submucosal myoma and even greater with an increased number of submucosal fibroids (HR=8,4, 95% CI= [2-29], p<0,01 in patients with one submucosal myoma but HR=12,7, 95% CI= [5-35] for two submucosal fibroids, p<0,01). (42) Our results correlate with these studies showing submucosal fibroids to increase complication rate, including failure of treatment. (60) However, our study did not reach such a high complication ratio. As they suggest, results could diverge depending on analyzing all fibroids or only the major fibroid. Cervical, lower body or front wall uterine fibroids show less infarction after UAE than other fibroids localization in the uterus. (61) Pedunculated subserosal fibroids are less attained by UAE, which could increase failures of treatment as well. (32) In parallel, submucosal fibroids show the greatest results in size regression after UAE. (62) (63) Incomplete infarction of fibroid could explain failure of treatment, hence a need of reintervention for symptomatic fibroids. (40) Near complete or partial (<90%) infarction of the dominant leiomyoma (OR=22.238; 95% CI=[2.405-205.620]; p = 0.006), as well as the presence of non-dominant viable leiomyomas (OR=12.134; 95% CI=[1.213-121.409]; p = 0.034) are possible independent risk factor of reintervention. (41) Likewise, we found that submucosal fibroids increased the risk of complications; dominated by reintervention.

Measured volume of fibroids with the imaging software was not related to UAE complications compared to mathematical formulas to evaluate their volume (p=0,07 and p<0,01). These formulas could be less precise, not following fibroids edges, increasing the difference between both estimating fibroids' volume's methods, and therefore

creating a false positive result. Retrospective studies did not correlate volume of fibroids over 10cm diameter to UAE complications. (43) (44) But giant fibroid (>10cm diameter) may be a risk factor of complication. (45) Likewise, literature is inconclusive on the safety to perform UAE on megauterus (>700cc or >1000cc). (45) (14) A prospective study concluded that megauterus could have a 20% rate of severe complications. (46) Fibroid localization and number of fibroids were not related to complication nor success rate with one-year insight in Firouznia et al. multivariate regression model. (47) Compared to us, they used only polyvinyl alcohol particles (PVA) of 500 to 710-mum; when we use these small sized particles with bigger ones (up to 1200mum).

The EMMY trial showed a dose effect response between the quantity of particles used during uterine artery embolization and fever (OR, 2.05; 95% CI, 1.09-3.87; P = 0.027), major complications (OR, 5.68; 95% CI, 2.05-15.75; P = 0.001), and high pain scores (OR, 1.97; 95% CI, 1.08-3.58; P = 0.027). (48) Another prospective study did not show size or particles quantity to be an infectious risk factor. (44)

3- Strengths

The major strength of our study is its originality. In literature, only one very recent case control study could be found researching risk factors of uterine artery embolization complications. (14) This case control focuses on infectious complications. UAE complications being a rare event, a case control study is the best-suited protocol to perform to identify risk factors. Using six different protocols probably did not permit us to acknowledge all of UAE complications in our center. The multiple protocols used to find cases show the difficulty to be comprehensive, however many methods are run to identify cases, in a retrospective study. Hence, as our study shows, retrospective studies cannot be thorough.

Loss to follow up is a classical limit in retrospective study. However, a case control protocol bypasses that bias. Furthermore, having researched and numbered the patients loss to follow up, we tried to reach comprehensiveness in our study.

Our study aims to have the best external validity as possible, using radiologic mathematical formulas combined to radiologist evaluation of fibroids volume and uterine volume, as well as adverse events validated classification.

4- Limits

Limits in our study include loss of information due to its retrospective nature. Especially for MRI and UAE procedures, losses of information could not be found in electronical charts. In addition, we cannot guarantee the comprehensiveness of the cases collected.

Ethnicity has been considered a potential risk factor of UAE complication: African American patients are at higher risk of complications. (49) (13) We were not able to collect this data. Ethnicity is not available in our electronical charts.

A main limit of our study was the impossibility to perform strong statistics using all potential risk factors due to missing data, especially on estimation of imaging volume. Our team of radiologists is currently reviewing all MRI to collect these data in order to complete our analysis.

Studying a rare complication, we used a composite primary outcome to maximize the number of patients included in our study. We minimized the number of adverse events included in our composite primary outcome measure aiming to limit our study on severe complications. However, different early complications and failure of treatment can have completely different presentation and might have different risk factors. We chose to pool all complications to maximize the incidence of cases, thus losing on risk factors specificity. Therefore, we are unable in our study to define specific risk factor for each complication. We can argue that differentiating symptomatic complications to failure of treatment could be a more specific method to identify risk factors of each complication. However, as seen in our study, many patients presented with multiple symptoms leading to a second embolization and surgery. Therefore, it seems difficult to isolate failures of treatment, which can be asymptomatic or resolved in emergencies. In parallel, a wider population is paramount to study risk factor of each different complication separately.

As every case control study does, our study is inclined to error due to selection bias. Matching control patients to cases aims to limit any confusion bias. Using this type protocol, classification biases are always possible. In our study, we cannot know if the patients were hospitalized or consulted in another hospital for any of the uterine artery complications. If that were true, the controls would be unknown cases in our study. In order to limit this bias, we paired cases and controls on place of residence.

The monocentric character of our study can be another limit. But, being a specialized center, our expertise makes the procedure uniform and more reproducible. Plus, it enables us to increase the incidence of patients treated in our center, being in a region with a low-density of doctors compared to the population.

5- Opening

Worldwide national guidelines differ mainly about the role of fibroid localization as a risk factor (submucosal, pedonculated) but not about other risk factors. (15) Risk factors start to be identified in literature like megauterus; while others remain unsure (BMI, localization or number of fibroids, submucosal localization). It would be interesting, in a near future, to include our study in a meta-analysis to evaluate the potential risk of having a submucosal fibroid.

In parallel, French guidelines consider UAE as a valuable alternative treatment for large fibroids or megauterus while literature stays unsure about it. (2) (3) The definition of megauterus remains questionable (700cc? 1000cc?). Furthermore, the larger the uterus the more pain the patient will experience post-embolization proportionally to fibroid ischemia. This pain could lead to surgery. In the end, surgery might be the safest definitive treatment in presence of a large uterus or fibroid. Futhermore, patients describe having a better quality of life 2 years after undergoing surgical treatment compared to UAE. (51)

Therefore, acknowledging complication risk factors might help counsel patients about the different possible treatments. And, in case of existing risk factors, practitioners could advise patients towards a surgical procedure to avoid surgery perform in emergency du to complications. (14) As to the Society of Obstetricians and Gynecologists of Canada (SOGC) writes: “Women who choose UAE as an alternative to hysterectomy should be counseled regarding the risk of major complications of UAE where hysterectomy may be

urgently required and potentially lifesaving. In view of this small but important risk, UAE is relatively contraindicated in women who are unwilling to have a hysterectomy under any circumstances." (50)

It is time to review our national guidelines on fibroid treatment and, in doing so, leveling them with other national guidelines.

# Conclusion

Uterine artery embolization is perceived as a safe and effective treatment of symptomatic uterine fibroids. Our specialized center reports a rate of complication and failure of treatment lower than the ones found in literature. (64) A precise selection of patients to undergo UAE might minimize overall complications.

Risk factors of UAE are still questioned in literature due to the retrospective nature of most studies. However, recently meta-analyses and case control studies, point to size of the uterus, number of fibroids and size of major fibroid as complications risk factors. Submucosal fibroids are recently questioned. Other meta-analyses are pursued and need to conclude on the subject. (65) Our study shows an important risk related to submucosal fibroids. Including it in a meta-analysis could be interesting to conclude on the subject.

International guidelines are unaware of these recent findings and would benefit of a renewal.

In the mean time, it is our duty as practitioners to wisely inform our patient of the risk of complications in presence of a megauterus or large and numerous fibroids, especially if one is submucosal. Surgery as an initial or emergency treatment must be discussed. Short and long-term survey must be organized if the patient choses to undergo uterine artery embolization. (66)

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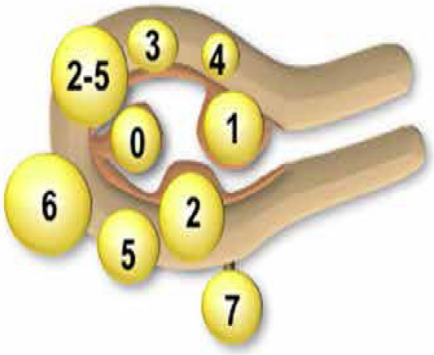
# Appendix

a. FIGO staging of fibroids

**Système de sous-classification des léiomyomes**




| | | |
|---|---|---|
| **S – Sous-muqueux** | 0 | Pédiculé, endocavitaire |
| | 1 | < 50 % intramural |
| | 2 | ≥ 50 % intramural |
| **A – Autres** | 3 | Est en contact avec l'endomètre; 100 % intramural |
| | 4 | Intramural |
| | 5 | Sous-séreux, ≥ 50 % intramural |
| | 6 | Sous-séreux, < 50 % intramural |
| | 7 | Sous-séreux, pédiculé |
| | 8 | Autre (à préciser, p. ex. cervical, parasitaire) |

| | | |
|---|---|---|
| **Léiomyomes hybrides** (affectent tant l'endomètre que la séreuse) | Deux des nombres sont liés par un trait d'union. Par convention, le premier de ces nombres désigne la relation avec l'endomètre, tandis que le deuxième désigne la relation avec la séreuse. Un exemple apparaît ci-dessous. | |
| | 2-5 | Simultanément sous-muqueux et sous-séreux, moins de la moitié du diamètre se trouvant à la fois dans la cavité endométriale et dans la cavité péritonéale |

b. SIR adverse event classification

Following Khalilzadeh O et al. *Proposal of a New Adverse Event Classification by the Society of Interventional Radiology Standards of Practice Committee.* J Vasc Interv Radiol JVIR. 2017 Oct;28(10):1432-1437.

i. Classification of 2003

**Table 1.** SIR Existing AE Classification (12)

| Category/Class | Definition |
|---|---|
| Minor complications | |
| A | No therapy, no consequences |
| B | Nominal therapy, no consequence; includes overnight admission for observation only |
| Major complications | |
| C | Requires therapy, minor hospitalization (< 48 h) |
| D | Requires major therapy, unplanned increase in level of care, prolonged hospitalization (> 48 h) |
| E | Permanent adverse sequelae |
| F | Death |

AE = adverse event.

ii. Classification of 2017

**Table 6.** Expanded Accordion Complication Classification (7)

| Grade | Definition |
|---|---|
| 1 | Mild complication; requires only minor invasive procedures that can be done at the bedside such as insertion of intravenous catheters, urinary catheters, and nasogastric tubes, and drainage of wound infections; physiotherapy and the following drugs are allowed: antiemetic, antipyretic, analgesic, diuretic agents, electrolytes, and physiotherapy |
| 2 | Moderate complication; requires pharmacologic treatment with drugs other than such allowed for minor complications, such as antibiotic therapy; blood transfusions and total parenteral nutrition also included |
| 3 | Severe complication; invasive procedure without general anesthesia; requires management by an endoscopic, interventional procedure, or repeat operation without general anesthesia |
| 4 | Severe complication; operation under general anesthesia; requires management by an operation under general anesthesia |
| 5 | Severe complication; organ system failure |
| 6 | Death |

Vu, le Directeur de Thèse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Tours, le

Dépôt de thèse signé

**De WIT Adeline**

73 pages – 8 tableaux – 6 figures – 3 annexes

**Résumé :**

**INTRODUCTION** L'embolisation des artères utérines (EAU) est réputée comme une alternative sûre et efficace à la chirurgie pour traiter les fibromes symptomatiques. Les facteurs de risques de complication ne sont pas clairement identifiés dans la littérature.

**METHODES** Nous avons réalisé une étude cas-témoins sur les dernières 15 années dans notre centre universitaire spécialisé. Toutes les complications au minimum de grade 2 selon les recommandations pour la pratique de la société de radiologie interventionnelle, correspondant à des complications sévères ou nécessitant une hospitalisation ont été colligées.

**RESULTATS** Parmi les 73 cas recensés, 24,7% ont été hospitalisés pour douleurs (n=18/73), 26% pour infection (n=19/73) et 2,74% ont expulsé leur fibrome (n=2/73). Au total, 35 patients ont eu recours à une deuxième ligne de traitement (47,9%), plus souvent chirurgical (n=18/35, 51,4%). L'analyse univariée (n=69) isolait l'immunosuppression (p=0,02), l'association DIU avec adénomyose (p=0,04), le volume du plus gros fibrome (p=0,04), la localisation sous-muqueuse d'un fibrome (p<0,01), l'estimation du volume utérin (p<0,01), le type et la quantité de particules utilisées (p=0,03) comme facteurs de risques potentiels. Seule la localisation sous-muqueuse (OR=4,84, IC95%=[1,95; 12,03], p<0,01) était indépendamment liée aux complications des UAE.

**CONCLUSION** Le seul facteur de risque indépendant de complication d'embolisation des artères utérines retrouvé est la présence d'un fibrome sous-muqueux (p<0,01). Il doit être pris en considération pour informer les patients, mettre en place leur surveillance et les conseiller sur de potentielles alternatives thérapeutiques.

**Mots clés :** facteurs de risque, embolisation, fibromes, sous-muqueux

**Jury :**

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