Nonoperative Management of Acute Upper Limb Ischemia

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Abstract

Background: Acute upper limb ischemia (AULI) is an uncommon emergency warranting immediate evaluation and treatment. The role of nonsurgical therapies including endovascular techniques, thrombolytics, and anticoagulation remains undefined. The authors systematically reviewed the current literature on the nonsurgical treatment of acute ischemia of the upper extremity. **Methods:** A PubMed and Embase search was conducted, and articles were screened using predetermined criteria. Data collected included patient demographics, cause of upper limb ischemia, type of nonsurgical treatment used, treatment outcomes, and complications. Patients were divided into 4 treatment groups: catheter embolectomy, catheter-directed thrombolysis, endovascular stenting, and anticoagulation/medical therapy alone. **Results:** Twenty-three retrospective studies met the search criteria. Of 1326 reported occlusions, 92% (1221) were attributed to thromboembolic disease. The second most common cause was iatrogenic (1.5%). Overall limb salvage rates were excellent with catheter embolectomy (862 of 882 cases, 97.7%) and catheter-directed thrombolysis (110 of 114 cases, 96.5%). Limb salvage rates were also high with anticoagulation/medical therapy (158 of 165 cases, 95.8%), but poor functional outcomes were more often reported. **Conclusions:** High-quality evidence to guide the nonsurgical treatment of AULI is lacking. Retrospective studies support the utility of catheter-based embolectomy and thrombolysis for distal ischemia. Whether a surgical or nonsurgical approach is taken, anticoagulation therapy remains a mainstay of both treatment and prevention of AULI. Because AULI patients often have underlying cardiac and/or systemic disease, a multidisciplinary approach is essential to minimize complications and prevent future occurrences.

Keywords: acute, hand, ischemia, upper limb

Introduction

Acute upper limb ischemia (AULI) is less common than acute lower limb ischemia. Based on historical data, the annual incidence of AULI has been reported as 1.3 cases per 100 000 patients, accounting for 2% to 18% of surgical procedures for critical limb ischemia.^{9,17,34,42} Unlike lower limb ischemia that primarily occurs as a complication of peripheral vascular disease, AULI is often caused by thromboembolic disease, trauma, or iatrogenic factors.^{12,15} Successful revascularization and limb salvage depend on timely diagnosis and localization of the arterial occlusion.

Vascular reconstruction is associated with morbidity and mortality that may be circumvented in select cases. The role of nonsurgical options such as endovascular techniques, thrombolytic agents, and anticoagulation therapy continues to evolve but remains poorly defined for upper extremity ischemia. Despite the relative abundance of research on

endovascular therapies for acute ischemia of the lower extremities, the literature discussing these modalities for upper extremity ischemia is sparse. The purpose of this study is to systematically review the English-language scientific literature on the nonsurgical treatment of AULI.

Overview of Nonsurgical Treatments

Nonsurgical options for AULI treatment include endovascular techniques (such as percutaneous catheter embolectomy, catheter-directed thrombolysis, and stents) and

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medical management (such as anticoagulation). A brief overview of each of these treatment options follows.

Fogarty et al revolutionized the treatment of acute arterial occlusion in 1963 with the introduction of intravascular balloon catheters capable of extracting arterial thromboemboli via a percutaneous approach.^{16,44} In addition to retrieval strategies, ablative techniques including mechanical thrombectomy aim to physically break up clots and have been used for thrombosed hemodialysis grafts and occlusive disease in larger vessels.¹⁹

Catheter-directed thrombolysis has gained increasing acceptance as a first-line therapy for acute lower limb ischemia, yet its role in upper extremity revascularization remains unclear.²² A recent review highlights its potential utility for acute and chronic ischemia of the hand.¹³ The thrombolytic agents most commonly used are streptokinase, urokinase, and recombinant tissue plasminogen activator. All three agents activate plasminogen and promote fibrinolysis but differ in their mechanism of action and safety profiles.^{26,32,35} Given the lack of comparative studies, a recent systematic review was unable to determine the optimal thrombolytic agent for peripheral artery occlusion.³⁷

Endovascular stents represent an alternative to surgery for the management of peripheral artery aneurysms, arteriovenous fistulas, and arterial perforations.⁵ Stent grafts can be balloon expandable or self-expandable and loaded with pharmacologic agents to further promote vascular patency.⁴⁹ Endovascular stents have been used to treat dissections and aneurysms causing upper limb ischemia, but these techniques have largely been utilized for large vessels proximal to the brachial artery.^{1,33}

Prior to the advent of catheters and stents, pharmacologic and supportive therapies were the primary treatments for AULI. Commonly used anticoagulants include heparin and warfarin. In addition, calcium channel blockers, phosphodiesterase inhibitors, topical nitrates, and botulinum toxin injections have been used with varying success to promote vasodilation and minimize tissue loss in vasospastic diseases.^{4,31,46} Supportive therapy typically consists of smoking cessation, improving cardiac output, hydration, warming techniques, and avoidance of vasopressors.

Materials and Methods

A literature search of the PubMed and Embase databases was conducted to identify all citations relating to nonoperative management of AULI. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines for systematic reviews were followed (Figure 1).²³ The following terms were used in the literature search: *acute upper limb ischemia, acute upper extremity ischemia, hand or forearm or arm or upper limb or upper extremity, and arterial and emboli*. Research (categorized as

Figure 1. Flow diagram of study selection detailing identification, screening, eligibility, and inclusion.

epidemiologic studies or scientific articles) and nonresearch (case reports or case series) articles from peer-reviewed journals and conference abstracts were retrieved. Only articles written in English were considered. Of the initial 2474 titles retrieved in the PubMed search and 3244 titles retrieved in the Embase search, 266 titles discussed AULI and a nonsurgical treatment strategy.

Study selection was performed through 2 levels of screening from February to April 2015. In the first level, abstracts were reviewed for the following exclusion criteria: studies containing less than 3 cases, studies that only included cases of surgical management, studies that were solely a literature review, studies that did not specify the type of embolectomy procedure performed (open surgical embolectomy vs percutaneous catheter embolectomy), and studies reporting AULI secondary to chronic occlusive disease, inflammatory vasculitis, or collagen disease. In the second level, all articles filtered through the first level were independently read in their entirety by 2 of the authors, and the same exclusion criteria were applied. Only studies that successfully passed both levels of screening were included in the analysis. Disagreements in screening were ultimately decided by the senior author (J.P.H.).

Of the initial 2474 titles retrieved in the PubMed search and 3244 titles retrieved in the Embase search, 266 titles discussed AULI and a nonsurgical treatment strategy based on screening criteria. The following data were extracted from each primary article if possible: author, year of publication, number of patients, cause of AULI, symptom duration prior to evaluation and treatment, nonsurgical treatment used, efficacy of the treatment, and complications.

Results

No prospective clinical studies or comparative studies were available. Twenty-three retrospective studies were identified using the search criteria for the systematic review (Table 1). In these studies, average patient age ranged from 43 to 78 years. Females were affected more often than males (58% vs 42%). Of 1326 reported arterial occlusions, 92% (1221) were attributed to thromboembolic disease. The second most common cause of arterial occlusion was iatrogenic (1.5%).^{28,36,39,43} Of 976 patients with thromboembolic occlusion, 752 cases (77%) were attributed to cardiac origin disease. The most frequent sites of thromboembolic occlusion were the brachial (48%) and axillary (15%) arteries. The radial artery was involved more often than the ulnar artery (5.7% vs 2.5%). Only 1 study analyzed smoking status; out of 109 patients with AULI, 39 patients (36%) were active smokers and 10 patients (9%) were former smokers.²⁴ The following sections are organized by treatment modality to highlight the best available evidence for each.

Percutaneous Catheter Embolectomy

Thirteen studies utilizing catheter embolectomy (Table 2) for AULI were included.^{6,10,12,17,18,21,24,27,42} Restoration of distal pulses or angiographic evidence of occlusion did not always correlate with clinical symptoms or limb salvage. Complication rates were inconsistently reported. Ricotta et al reported that chronic paresthesias were present in 3 of 15 patients (20%) with catheter-induced AULI.³⁶ Hernandez-Richter et al reported that 6 of 111 long-term patients (5.1%) had arm pain only with heavy exercise, whereas the remainder had no or minimal symptoms with exercise. Licht et al reported that 9 of 57 patients (13%) had slightly decreased arm function and 2 (3%) had severe functional defects that did not correlate with symptom duration prior to intervention.²⁴ In contrast, another study reported that delayed presentation (13 hours) was associated with permanent loss of arm function in 1 patient.¹⁰ Overall, limb salvage was excellent (862 of 882 cases, 97.7%).

Hernandez-Richter et al reported a local complication rate of 20% due to wound infection or hematoma,¹⁸ and Kim et al described 1 patient with a large hematoma at the groin access site that required endovascular stenting.²¹ Stonebridge et al reported that failed embolectomy prompted surgical revascularization in 3 of 50 patients (6%), all with successful outcomes.²¹ Repeat embolectomies were needed in 22 patients (9%) in 1 study and recurrent embolic disease in the cerebral, gastrointestinal, and lower limb vasculature was detected in 10 of 21 patients (48%).^{18,28} In-hospital and long-term mortality were not consistently reported, but deaths were often attributed to cardiovascular or cerebrovascular disease.

Catheter-Directed Thrombolysis

Eight studies using catheter-directed thrombolysis (Table 2) were included.^{2,7,9,11,29,40,41,47} Thrombolysis was often used in conjunction with catheter embolectomy, particularly in the setting of worsening symptoms, proximal (subclavian/axillary) disease, or technical failure.^{2,41,47} In a series of 40 patients who underwent thrombolysis with concomitant heparin, greater success (75%, 9 of 12 patients) was achieved treating proximal occlusion at the subclavian/axillary/brachial artery compared with hand-level occlusion (33%, 4 of 12 patients).⁹ Long-term recurrence rates were generally low with follow-up ranging from 1 month to 5 years. Overall limb salvage rate was excellent (110 of 114 cases, 96.5%).

Common complications included catheter-associated hematomas and thromboses, technical failures due to inability to place catheter, and cerebral transient ischemic attacks.^{9,11,40,47} Higher complication rates were reported in a series of 5 patients with AULI due to unintentional intra-arterial injections.⁷ Two patients (40%) developed compartment syndrome after flow restoration (requiring hand or forearm fasciotomies), 1 patient required amputation in 3 distal phalanges, and 1 patient developed septic arthritis of the thumb interphalangeal joint requiring arthrodesis and bone grafting.

Stents/Stent Grafts

Studies reporting the use of stents for AULI are limited. Only 1 study met inclusion criteria for this review. Carrafiello et al treated 11 patients with AULI due to trauma at the subclavian, axillary, or brachial artery level.⁸ Stent grafts were used to treat pseudoaneurysms or transections in 8 patients. Balloon angioplasty was used to treat 2 cases of axillary artery occlusion and 1 case of axillary artery mural hematoma. There were no major complications and 1 case of incomplete radial artery thrombosis that resolved with oral anticoagulation. At long-term follow-up (mean 45 months), there was 1 stent graft occlusion that required intra-arterial thrombolysis. The overall primary success rate was 95% with a secondary success rate of 100% and no mortality.

Anticoagulation and Medical Therapy

Nine studies using anticoagulation and/or medical therapy (Table 2) alone were included.^{2,3,10,17,27,36,39,42,43} In general, indications for medical management included either mild symptoms or patients deemed too sick for invasive interventions. A study from the pre-endovascular era demonstrated considerable morbidity with the medical treatment of AULI.³ Twenty-two of 78 medically treated patients received anticoagulation or brachial plexus/stellate

Table 1. Pooled Analysis of Included AULI Studies.

Authors	Year of study	No. of patients	Average age	Sex distribution	Duration of symptoms	Cause of occlusion	Site of occlusion
Baird and Lajos	1964	95	60	M: 56 F: 39	Not specified	Thromboembolism, n = 102	Subclavian, n = 10 Axillary, n = 23 Brachial, n = 65 Radial, n = 2 Ulnar, n = 2
MacGowan et al	1973	24	Indeterminate (combined with LE patients)	Indeterminate (combined with LE patients)	Average 12-72 hours, with one exception of 4 days	Thromboembolism, n = 24	Subclavian, n = 2 Axillary, n = 3 Brachial, n = 17 Radial, n = 2
Champion et al	1973	7	60	M: 1 F: 3	Average of 6 hours, range 2.5-9 hours	Thromboembolism, n = 7	Axillary, n = 3 Brachial, n = 4
Savelyev et al	1977	256	62.7	M: 87 F: 169	Most patients admitted before 24 hours, range 2-3 months	Thromboembolism, n = 260	Subclavian, n = 46 Axillary, n = 66 Brachial, n = 142
Ricotta et al	1983	76	Not specified	Not specified	Not specified	Thromboembolism, n = 44 iatrogenic, n = 19 Thoracic outlet syndrome, n = 5 Arteritis, n = 3 Other, n = 5	Radial and/or ulnar, n = 3 Not specified, n = 3 Subclavian, n = 1 Axillary, n = 6 Brachial, n = 34 Radial, n = 3 Not specified, n = 32
Galbraith et al	1985	31	Indeterminate (combined with LE patients)	Indeterminate (combined with LE patients)	Average 71 hours, range 1 hour-30 days	Thromboembolism, n = 31	Axillary, n = 13 Brachial, n = 16 Radial, n = 1 Ulnar, n = 1
Sicard et al	1985	3	Indeterminate (combined with LE patients)	Indeterminate (combined with LE patients)	10 hours, 3 days, one patient not specified	Thromboembolism, n = 3	Brachial, n = 2 Graft (unknown), n = 1
Stonebridge et al	1989	61	74	M: 23 F: 51	Not specified	Thromboembolism, n = 61	Subclavian, n = 10 Axillary, n = 25 Brachial, n = 23 Distal, n = 2
Wildus et al	1990	8	52	M: 6 F: 2	2 hours-30 days	Thromboembolism, n = 3 iatrogenic, n = 1 Thoracic outlet syndrome, n = 1 Other, n = 3	Not specified, n = 1 Subclavian, n = 1 Axillary, n = 1 Brachial, n = 4 Radial, n = 1 Graft (subclavian), n = 1

(continued)

Table 1. (continued)

Authors	Year of study	No. of patients	Average age	Sex distribution	Duration of symptoms	Cause of occlusion	Site of occlusion
Michaels et al	1993	7	68	M: 3 F: 1	5 hours to several weeks	Thromboembolism, n = 4 Unknown, n = 3	Brachial, n = 4 Not specified, n = 3
Coulon et al	1994	13	63.6	M: 4 F: 9	2 hours -3 weeks	Thromboembolism, n = 13	Subclavian, n = 3 Axillary, n = 4 Brachial, n = 4 Radial, n = 2 Subclavian, n = 4 Axillary, n = 2 Brachial, n = 13 Digital, n = 1
Baguneid et al	1999	21	68	M: 6 F: 15	9.6 hours -14 days	Thromboembolism, n = 20 Unknown, n = 1	Not specified, n = 1 Axillary, subclavian, or isolated brachial, n = 3 Brachial including trifurcation, n = 9 Forearm, n = 16 Hand, n = 12 Not specified, n = 64
Cejna et al	2001	38	Male average 65, female average 62	M: 15 F: 23	1-14 days	Thromboembolism, n = 30 Thoracic outlet syndrome, n = 1 Arteritis, n = 2 Other, n = 7	Thromboembolism, n = 39 Thoracic outlet syndrome, n = 4 Arteritis, n = 15 Other, n = 6
Sultan et al	2001	64	51	M: 26 F: 38	Not specified	Thromboembolism, n = 39 Thoracic outlet syndrome, n = 4 Arteritis, n = 15 Other, n = 6	Subclavian, n = 10 Axillary, n = 21 Brachial, n = 185 Radial, n = 58 Ulnar, n = 28 Not specified, n = 14
Hernandez-Richter et al	2001	251	73	M: 102 F: 149	120 patients within 12 hours, 36 patients 12-18 hours, 10 patients 24 hours, 10 patients 2 days, 9 patients 3 days, 6 patients >10 days, 59 patients unknown (majority within 12 hours or unknown)	Thromboembolism, n = 316	Not specified, n = 148
Licht et al	2004	148	78	M: 54 F: 94	72 patients within 12 hours, 37 patients 12-24 hours, 38 patients >24 hours	Thromboembolism, n = 148	Not specified, n = 148
Deguara et al	2005	61	72.4	M: 29 F: 32	Not specified	Thromboembolism, n = 61	Subclavian, n = 3 Axillary, n = 6 Brachial, n = 52

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Table 1. (continued)

Authors	Year of study	No. of patients	Average age	Sex distribution	Duration of symptoms	Cause of occlusion	Site of occlusion
Bang and Nalachandran	2009	8	49-86	M: 1 F: 7	2-24 hours, with one exception of 2 days	Thromboembolism, n = 8	Not specified, n = 8
Magishi et al	2010	21	73	M: 14 F: 7	Average 9.7 hours, range 2-41 hours	Thromboembolism, n = 21	Axillary, n = 4 Brachial, n = 17
Carrafiello et al	2011	11	49.9	M: 7 F: 4	Not specified	Other, n = 11	Subclavian, n = 3 Axillary, n = 6 Brachial, n = 2
Kim et al	2011	11	74.5	M: 7 F: 4	Average 2.2 days, range, 0-4 days	Thromboembolism, n = 11	Axillary, n = 3 Brachial, n = 8
Schrijver et al	2011	28	60	M: 6 F: 22	Not specified	Thromboembolism, n = 15 Thoracic outlet syndrome, n = 4 Other, n = 1 Unknown, n = 8 Other, n = 5	Subclavian, n = 8 Brachial, n = 6 Radial and/or ulnar, n = 11 Graft (bypass), n = 3 Not specified, n = 5
Breguet et al	2014	5	43.4	M: 5 F: 0	Average of 68 hours, range 4-168 hours	Total occlusions: 1326 Thromboembolism: 1221 (92.1%) Iatrogenic: 20 (1.5%) Thoracic outlet Syndrome: 15 (1.1%) Arteritis: 20 (1.5%) Other: 38 (2.9%) Unknown: 12 (0.9%)	For thromboembolic occlusions (n = 1221): Subclavian: 89 (7.3%) Axillary: 179 (14.7%) Brachial: 588 (48.1%) Radial: 69 (5.7%) Ulnar: 31 (2.5%) Radial and/or ulnar: 3 (0.2%) Graft: 1 (0.1%) Distal: 2 (0.2%) Digital: 1 (0.1%) Not specified: 258 (21.1%)
Total	—	1,248	—	M: 365 (42.2%) F: 500 (57.8%)	—		

Note. AULI, acute upper limb ischemia; LE, lower extremity.

Table 2. Embolectomy, Thrombolysis, and Medical Treatment Studies.

Embolectomy study	Year	Patients treated	Immediate success (restoration of flow)	Long-term function/outcome	Complications	Limb salvage
MacGowan et al	1973	20 (20 cases)	Not reported	Not reported	Not reported	20 of 20 cases (100%)
Champion et al	1973	6 (6 cases)	Radial pulse restored in 3 patients (50%)	Return to full function in 5 patients, loss of function in 1 patient who received embolectomy greater than 13 hours after onset of symptoms	Not reported	6 of 6 cases (100%)
Savelyev et al	1977	206 (210 cases)	Radial or ulnar pulse restored in 134 cases (63.8%)	Not reported	The hospital mortality for those treated with approach outside the cubital fossa was 21.78%, and in the group operated on by means of the antecubital approach it was 19.04%; 21 patients developed gangrene, resulting in 11 amputations. One early occlusion in the catheter injury group	199 of 210 cases (94.8%)
Ricotta et al	1983	46 (40 simple embolectomy, 6 angioplasty cases)	In patients with cardiac emboli (n = 31), pulses restored in 30. Restoration of pulses not reported for patients with catheter injury (n = 15).	In patients with cardiac emboli (n = 31), none complained of chronic arm pain or loss of function. Mortality rate was 12% (4 of 31), attributable to atherosclerotic or cardiac disease. In patients with catheter injury (n = 15), 3 patients (20%) complain of chronic paresthesias.	One early occlusion in the catheter injury group	46 of 46 cases (100%)
Galbraith et al	1985	25 (25 cases)	Not reported	2 patients with claudication, 1 with nerve palsy, 21 asymptomatic	1 patient died before discharge, no cause reported	25 of 25 cases (100%)
Stonebridge et al	1989	50 (50 cases)	Not reported	Mortality rate was 5% (3 patients, one due to pulmonary embolus). Return to full function of the upper limb in all 58 patients who survived, but unable to distinguish from patients who received conservative treatment.	3 patients required additional vascular reconstruction	50 of 50 cases (100%)
Sultan et al	2001	21 (21 cases)	Not reported	Good outcome in 18 patients, poor outcome in 3 patients (14.3% mortality); 4 patients with stroke (19%)	Not reported	Amputation occurred in 10 of 64 overall AULI cases (15.6%), but unable to distinguish which amputations occurred postembolectomy.
Hernandez-Richter et al	2001	251 (283 cases)	Not reported	30-day postoperative mortality was 5.6%. At long-term follow-up, 111 of 117 living patients (94.9%) had no complaints or minor coldness and pain following heavy exercise. In 6 cases (5.1%), heavy exercise-induced pain was observed in the treated extremity.	In 182 cases (72.5%), no complications occurred postoperatively. In 18 cases (7.2%), general medical complications such as heart failure or stroke occurred. In 51 cases (20.3%), local complications such as wound infection or hematoma occurred. In 22 cases (8.8%), re-occlusion of the affected artery occurred.	278 of 283 cases (98%) in the postoperative period.
Licht et al	2004	148 (138 simple embolectomy, 5 embolectomy and vascular reconstruction, 5 embolectomy and intraoperative thrombolytics)	Radial pulse restored in 133 patients (90%), ulnar pulse restored in 85 patients (57%)	30-day mortality was 9% (14 patients), attributable to 4 heart failures, 4 respiratory failures, 3 strokes, 2 gastrointestinal bleeds, and 1 tumor cachexia; 68 survivors participated in long-term follow-up (median 29 months); 57 patients had a normal arm function (84%). 9 patients (13%) had slightly decreased arm function, and 2 patients (3%) had severely decreased arm function.	Satisfactory result achieved in 134 cases; 7 patients (4.7%) underwent re-embolectomy during hospital stay, of which 2 ultimately required amputation.	On long-term follow-up (mean 1293 days), 4 of 117 patients had amputations of the affected limb. 146 of 148 cases (98.6%)

(continued)

Table 2. (continued)

Embolectomy study	Year	Patients treated	Immediate success (restoration of flow)	Long-term function/outcome	Complications	Limb salvage
Deguara	2005	55 (52 simple embolectomy, 3 embolectomy and fasciotomy)	Not reported	No patients had evidence of arterial occlusion at follow-up (median 9 months). The 30-day mortality was 18.2% (n = 10), attributable to cardiopulmonary causes.	Two patients required repeat embolectomy. Unable to distinguish other complications from patients treated with thrombolysis or stent/angioplasty.	55 of 55 cases (100%)
Bang and Nalachandran	2009	8 (8 cases)	All patients had good backflow and palpable radial pulses postoperatively	At time of discharge, outcomes good in 7 patients. Long-term outcome data not reported.	One patient developed recurrent embolic event after the first procedure and had a subsequent revascularization procedure, which was unsuccessful and led to amputation. One patient developed a postoperative brainstem stroke and was terminally ill when discharged.	7 of 8 cases (87.5%)
Magishi et al	2010	21 (21 cases)	20 cases showed no angiographic stenosis or obstruction of the arteries in the forearm, but 1 showed obstruction of the radial artery and stenosis of the palmar arch.	On long-term follow-up (median 20.2 months), none of the patients developed upper limb re-occlusion after the first operation. Cause of death was cerebral infarction in 4 cases, heart failure in 2, supramesenteric artery embolism in 1, and lower extremity embolism in 1.	Posttreatment re-embolism occurred in 10 cases, cerebral infarction in 8, supramesenteric artery embolism in 1, and lower extremity artery embolism in 1. Three of these cases occurred within a week after the operation.	21 of 21 cases (100%)
Kim et al	2011	10 (6 PAT, 4 PAT and thrombolysis)	Technical success, defined as the restoration of continuous inline flow through the brachial artery, and superficial and deep palmar arch, achieved in all patients	One patient died of congestive heart failure 2 months after the procedure. On follow-up (mean 7.2 months) Doppler examination, no thrombus was observed in either the brachial or axillary artery. Seven patients with residual emboli in the radial or ulnar artery on final angiography, excluding one patient, who died of congestive heart failure, did not show residual emboli on color Doppler ultrasound after 1 to 3 months and were asymptomatic. One patient had a stroke, and 2 developed lower leg ischemia due to embolic disease.	One patient developed a massive groin access site hematoma requiring percutaneous stent and 1 patient developed re-occlusion of the brachial artery from excess compression of access site, as detected on ultrasound, but was asymptomatic and did not require additional treatment.	10 of 10 cases (100%)
Total embolectomy limb salvage rate: 862 of 882 cases (97.7%)						
Thrombectomy study	Year	Patients treated	Immediate success (restoration of flow)	Long-term function/outcome	Complications	Limb salvage
Sicaud et al	1985	3 (3 cases)	Not reported	One patient had a successful outcome, 1 patient required amputation, 1 patient experienced clot migration, worsening ischemia, and thrombectomy.	Minor complications occurred at a rate of 42% (18 of 43 treatments), and major complications occurred at a rate of 44% (19 of 43 treatments), but unable to distinguish UE from LE complications.	2 of 3 cases (67%)
Wildus et al	1990	8 patients (9 cases)	On angiography, 3 patients had excellent flow through all arm vessels. Two patients had 1-cm proximal ulnar artery occlusions, whereas 1 had a focally occluded radial artery that was recanalized. One patient was left with an occluded radial artery. Angiography was not performed on one patient.	All regained radial or ulnar flow to hand initially. On 4-month follow-up, 1 patient died from congestive heart failure, 2 experienced clot recurrence, 2 underwent operative procedures, 1 had thoracic outlet syndrome, and 2 patients had no recurrence.	Distal clot migration occurred 4 times: in both cases of subclavian thrombolysis and the cases of axillary artery occlusion and brachial graft thrombosis. Two patients developed puncture-site hematomas, one requiring operative evacuation.	9 of 9 cases (100%)
Michaels et al	1993	4 (4 cases)	Distal pulses returned in 2 patients (50%), thrombus dissolution achieved in all patients.	All patients were asymptomatic at long-term follow-up (mean 6.5 months, 3-12 months).	None reported	4 of 4 cases (100%)

(continued)

Table 2. (continued)

Thrombectomy study	Year	Patients treated	Immediate success (restoration of flow)	Long-term function/outcome	Complications	Limb salvage
Coulon et al	1994	13 (13 cases)	Angiography showed complete arterial clearing in 8 patients, and minor residual proximal clots or subtotal distal clearing in 5 patients.	11 patients became asymptomatic, 1 patient continued to have numbness of the fourth and fifth fingers, and 1 patient result considered satisfactory given multiple atheromatous lesions were present. No limb ischemia recurred during a follow-up of 1 to 5 years.	Transient ischemic attack (n = 1), catheter-associated hematoma (n = 7)	13 of 13 cases (100%)
Baguneid et al	1999	12 (12 cases)	Three technical failures, subsequently treated with embolotherapy. Of the 9 patients who underwent thrombolysis, 6 had complete lysis and resolution of symptoms and 1 had partial lysis and relief of rest pain. Thrombolysis failed in 2 patients with one undergoing a successful embolotherapy, and one undergoing bypass surgery.	No recurrence of upper limb ischemia at a median follow-up of 18 months	One patient developed hemiplegia 24 h after commencing thrombolysis but regained function at 6-month follow-up.	12 of 12 cases (100%)
Cejina et al	2001	40 (40 cases)	Overall success rate defined as complete recanalization was 55%. The lysis results for isolated upper arm, combined brachial and forearm occlusions, and forearm and hand artery occlusions were 100%, 55%, and 46%, respectively. Of 18 patients who failed thrombolysis, 8 underwent embolotherapy and 10 were treated with oral anticoagulation.	Clinical improvement, defined as relief of ischemic symptoms and lack of amputation, after thrombolysis and medical therapy was achieved in all cases at 12-month follow-up.	One large puncture-site hematoma in the groin required surgery. Three distal pericatheter thromboses occurred, of which 1 required surgery.	40 of 40 cases (100%)
Schrijver et al	2011	28 (28 cases)	Complete lysis was achieved in 17 patients and partial lysis was achieved in 4 patients (75%); 7 patients failed thrombolysis, and were treated with embolotherapy (n = 4), amputation (n = 2), and conservatively (n = 1).	The patients who were treated successfully with thrombolysis achieved complete resolution of symptoms. At 1-month follow-up, 2 re-occlusions were treated successfully with angioplasty (n = 1) and thrombolysis (n = 1).	The placement of thrombolysis catheter was unsuccessful in 1 patient; 1 patient had a thromboembolic complication of the lower limb, and 1 had a transient ischemic attack.	26 of 28 cases (92.9%)
Breguet et al	2014	5 (5 cases)	In-line flow to the affected hand was restored in all patients, leading to a technical success rate of 100%	One patient had necrosis of distal phalanges and subsequent amputation, 1 patient experienced aseptic arthritis of interphalangeal articulation, requiring surgery, and 3 patients had resolution of symptoms.	Two patients developed compartment syndrome of the hand or forearm requiring fasciotomies.	4 of 5 cases (80%)
Total thrombectomy limb salvage rate: 110 of 114 cases (96.5%)						
Medical treatment study	Year	Patients treated	Immediate success (restoration of flow)	Long-term function/outcome	Complications	Limb salvage
Baird and Lajos	1964	78	Not reported	In total, 56 patients received supportive therapy alone—36 patients (64%) had no recurrence of symptoms, 17 (30%) had significant disability, and 3 (6%) resulted in amputation. Twenty-two patients received anticoagulation or nerve block—17 (77%) had no recurrence of symptoms, 2 (10%) had significant disability, and 3 (13%) resulted in amputation.	Not reported	72 of 78 cases (92.3%)

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Table 2. (continued)

Medical treatment study	Year	Patients treated	Immediate success (restoration of flow)	Long-term function/outcome	Complications	Limb salvage
Champion et al	1973	1	Radial pulse palpable at discharge	Motor function restored at discharge. The patient died 3 months later from a cerebral embolus.	Not reported	1 of 1 case (100%)
MacGowan et al	1973	4	Not reported	Not reported	Not reported	4 of 4 cases (100%)
Savelyev et al	1977	47	Restoration of radial pulsation at the wrist in 9 patients	Not reported	The hospital mortality rate of patients treated conservatively was 23.4%. Gangrene developed in 1 patient, resulting in patient death.	47 of 47 cases (100%)
Ricotta et al	1983	13	Not reported	Seven of 44 patients (30%) deemed unfit for surgery died within 36 hours of evaluation, 5 patients showed gradual improvement, 1 patient presented with gangrene that required amputation.	None reported	12 of 13 cases (92.3%)
Galbraith et al	1985	6	Not reported	Three patients (50%) had persistent arm pain on exercise, and 3 patients (50%) were asymptomatic at discharge.	Not reported	6 of 6 cases (100%)
Stonebridge et al	1989	11	Not reported	Not reported	Not reported	11 of 11 cases (100%)
Baguneid et al	1999	5	Not reported	Five patients were treated conservatively with heparin followed by warfarin, resulting in 3 partial and 2 complete recoveries. The patient selected for intravenous prostacyclin infusion also experience complete resolution of symptoms.	Not reported	5 of 5 cases (100%)
Sultan et al	2001	17	Not reported	Long-term functional outcomes not reported. Majority of patients had nonspecific arthritis—4 treated with plasmapheresis, 5 had good response to corticosteroids, colchicine, and calcium channel blockers, 3 had poor results with corticosteroids and cytotoxic agents, 3 had very poor results with corticosteroids and colchicine.	Not reported	Overall amputation in 10 cases, but unable to distinguish from patients who underwent embolectomy
Total medical treatment limb salvage rate: 158 of 165 cases (95.8%)						

Note. AULI, acute upper limb ischemia; PAT, percutaneous aspiration thromboembolectomy; LE, lower extremity; UE, upper extremity.

ganglion block or both, resulting in 3 patients (13%) with a nonfunctional arm or requiring amputation. The remaining 56 medically treated patients received supportive therapy only (warming, “chemical vasodilators”). Overall, 25 of the 78 medically managed patients (32%) were left with a disabled arm and 6 patients (8%) required an amputation.

Savelyev et al treated 47 patients with arterial emboli conservatively.³⁹ These patients generally had mild symptoms that improved with medical therapy (heparin, anti-spasmodics, improving cardiac output) or were too sick for surgery or refused surgery. Nine of these patients (19%) regained a radial pulse and gangrene developed in only 1 patient (2%). However, 37 patients (79%) continued to suffer from functional deficits despite avoiding limb amputation. Similarly, 3 of 6 AULI patients (50%) managed conservatively by Galbraith et al suffered from persistent arm pain after exercise.¹⁷

Ricotta et al managed 13 of 44 AULI patients (30%) presenting with cardiac emboli with conservative treatment consisting of observation with or without anticoagulation therapy.³⁶ Seven patients were unfit for surgery and 4 died within 36 hours of evaluation (30% mortality). Five patients were observed and showed gradual improvement, and 1 patient presented several weeks after the initial event with gangrene requiring digital amputation. Recent studies have reported variable outcomes combining heparin therapy with prostacyclin, plasmapheresis, steroids, immunosuppression, and calcium channel blockers for AULI.^{2,43}

Discussion

The management of AULI is challenging due to its rarity, variable presentation, wide array of etiologies, and lack of evidence-based guidelines. A detailed history and physical are essential to direct initial care and should be supplemented by diagnostic exams such as ultrasonography and computed tomography (CT) as necessary. Angiography remains the gold standard diagnostic tool, particularly for hand and digit ischemia, and permits therapeutic intervention.⁴⁸ Treatment strategies continue to evolve with the introduction of novel endovascular devices and targeted pharmacologies.²⁵

As confirmed in this review, a majority of AULI cases are due to thromboembolic disease that often localizes to proximal arm vessels and are amenable to embolectomy techniques. Outcomes are generally excellent, accounting for an overall limb salvage rate of 97.7% (862 of 882 cases). However, an experienced interventional radiologist or reconstructive surgeon must be available to initiate treatment. Strong consideration should be made to transfer these patients to a tertiary care center with available endovascular and surgical resources. Pooled analysis demonstrated that 77% of thromboembolic cases could be attributed to cardiac disease (eg, atrial fibrillation and valvular disease), highlighting the

importance of a cardiac workup as indicated. Recurrent upper limb emboli appear to be a poor prognostic indicator and may represent untreated proximal (cardiac or thoracic arch origin) and/or systemic disease.^{18,42}

Catheter-directed pharmacologic thrombolysis also demonstrates excellent clinical results for AULI with a limb salvage rate of 96.5% (110 of 114 cases). Thrombolysis may allow time for the distal ischemia to “declare itself” while potentially limiting further tissue loss. These techniques may be better suited for distal occlusions that cannot be effectively reached with balloon or stent devices. Complication rates are not insignificant, and close monitoring for both local (access site hematomas) and distant (cerebrovascular accidents) hemorrhagic complications is imperative. Mechanical thrombectomy devices have been used to treat upper extremity dialysis graft occlusion, but their use for occluded forearm or hand vessels has not been described.⁴⁵

Endovascular stents have not been reported to treat non-traumatic AULI. Although promising results have been published for traumatic injury to larger upper extremity vessels, stent technology for hand ischemia has been restricted to case reports with short-term follow-up.^{14,30} Angioplasty techniques have been utilized in distal vessels and appear useful as temporizing measures in chronically ill patients.²⁰ Long-term patency of small vessel stents may be enhanced with drug-eluting technology, but its use for AULI has not been described.³⁸

Anticoagulation remains a mainstay of treating ischemia of the upper and lower extremities and can be rapidly initiated in the absence of contraindications (recent or active bleeding). It is often used concomitantly with thrombolysis to minimize catheter-associated clot formation and may reduce clot propagation in existing thromboses. In general, it is advocated as a salvage option in patients too sick for surgical/endovascular therapy or for those with mild symptoms that are either improving or stable. Importantly, anticoagulation plays a critical role in preventing recurrence of thromboembolic disease.

The limitations of the present study include those inherent in systematic reviews based on retrospective studies. Studies lacked adequate control groups, used highly variable outcome measures, and included historic data spanning over 5 decades. Specific details regarding patient demographics, treatment algorithms, and surgical details were routinely missing. The degree of functional impairment was often not described, and older studies commonly reported qualitative outcomes.

Given the lack of evidence-based guidelines, the evaluation and management of AULI remain largely based on expert opinion, surgeon training, and institutional resources. A key treatment branch point is in determining whether the ischemia is acute or chronic as early AULI may be more amenable to nonsurgical intervention. A thorough history should reveal onset, duration, and progression of symptoms

or a history of similar symptoms in the past. The abrupt presentation of worsening pain and coolness suggests an acute source. A history of peripheral vascular disease, heart arrhythmia, hypercoagulable state, connective tissue disease, smoking, or injectable drug use may also suggest an acute embolic source or acute thrombosis. In contrast, intermittent symptoms, claudication and rest pain or a long-standing history of cold intolerance, Raynaud phenomena, or scleroderma may point to chronic disease that may not warrant immediate intervention.

Comparisons with the contralateral limb and/or adjacent unaffected digits are paramount. Reassuring exam findings include the presence of palpable pulses at the wrist and Doppler signals in the digit tips. In addition, upper extremity compartments should be soft and motor-sensory function intact. Lack of hair, atrophy, and fibrotic skin changes may suggest chronic digit ischemia. The level of suspected occlusion is key as more proximal blockages may be amenable to endovascular therapy. Sharp demarcations between warm and cool tissues suggest an acute embolic event. The lack of distal pulses or Doppler signals in a cool extremity with impaired function mandates an aggressive diagnostic and therapeutic approach.

Angiography remains the diagnostic gold standard but may not be readily available. If angiography is not readily available and a limb clearly exhibits critical ischemia, a CT angiogram may help with localizing disease prior to emergent surgery. However, if interventional radiology is available, critically ischemic limbs that appear salvageable should be brought promptly to the angiography suite for imaging and possible endovascular therapy. Angiography findings of diffuse vessel pathology, thrombus with concavity toward the lumen, and extensive collateralization strongly suggest chronic disease, whereas proximal aneurysmal disease, thrombus convex toward the lumen, and otherwise healthy normal-appearing vessels may suggest acute embolism. If endovascular therapy is performed, close inpatient monitoring is required as reperfusion injury may lead to compartment syndrome. Any concerns for compartment syndrome should be addressed with prophylactic fasciotomies whether endovascular modalities are used or not.

In summary, nonsurgical approaches for AULI are an important option for surgeons treating upper limb ischemia. Current advances in endovascular and antithrombotic therapy have the potential to improve outcomes for AULI while minimizing surgical morbidity. Close collaboration between hand surgery, vascular surgery, and interventional radiology is imperative to optimize outcomes. Additional consultation with medical specialists including cardiology, hematology, and rheumatology is also warranted to assist in treating cardiac and/or systemic disease and minimizing medical morbidity.

Authors' Note

Victor W. Wong and Melanie R. Major contributed equally to this article.

Ethical Approval

This study was approved by our institutional review board.

Statement of Human and Animal Rights

A statement of human and animal rights is not applicable to this article because this is not a research study and there was no human or animal experimentation.

Statement of Informed Consent

Because this is a systematic review with no identifiable patient information, no informed consent was needed.

Declaration of Conflicting Interests

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