UAB
Universitat Autònoma de Barcelona

Dipòsit digital de documents de la UAB

This is the **accepted version** of the journal article:

Casajuana Urgell, Eduard [et al.]. «Acute limb ischemia in nonagenarians : Characteristics and factors related to outcomes in a single-center consecutive series». *World Journal of Surgery*, Vol. 48, Num. 1 (January 2024), p. 240-249 DOI 10.1002/wjs.12021

This version is available at https://ddd.uab.cat/record/330436

under the terms of the IN COPYRIGHT license.

Acute Limb Ischemia in Nonagenarians: Characteristics and Factors Related Outcomes in a single-center consecutive series

Eduard Casajuana Urgell[1,2] MD, Laura Calsina[1,3] MD, PhD., Maria Mascaró Oliver[1] MD, Mar Abadal Jou[1] MD, Albert Clarà Velasco[1,3,4] MD, PhD.

[1] Department of Vascular Surgery, Hospital del Mar, Barcelona, Spain

[2] Department of Surgery, Universitat Autònoma de Barcelona, Barcelona, Spain

[3] Department of Life and Health Sciences, Universitat Pompeu Fabra, Barcelona, Spain

[4] CIBER Cardiovascular, IMIM – Parc de Salut Mar, Barcelona, Spain

Word count (main text): 2255

Corresponding author: Albert Clarà Velasco, MD, PhD

*Department of Vascular Surgery, Hospital del Mar, Barcelona, Spain

*Mailing address: Passeig Marítim 25-29, 08003 Barcelona, Spain

*Phone number: +34 932483222; Email address: aclara@psmar.cat

Keywords: Acute limb ischemia; Nonagenarians; Revascularization.

Conflict of Interest: The authors declare that they have no conflict of interest.

The study was conducted with the approval of the Institutional Human Research Ethics Committee (CEIC/PSMAR).

ABSTRACT

Background: The increasing aging and frailty of the population make the management of acute limb ischemia more difficult, with decision-making far from being guided by evidence. The aim of the study was to evaluate the characteristics and results of acute ischemia treatment in nonagenarians.

Materials and Methods: Retrospective analysis of a consecutive series of nonagenarian patients with ALI attended at our institution between 2008 and 2021. The primary outcomes of the study were 1-year limb salvage and survival rates.

Results: A total of 102 patients were included (mean age 92.38, 78.4% women). In 83 cases (81.4%) ALI was attributed to embolism, and 19 (18.6%) to acute arterial thrombosis. Fifteen patients (14.7%) were treated palliatively, including 8 (53.3%) irreversible ALI with associated malignancy/advanced dementia, 5 (33.3%) with associated cerebral/intestinal ischemia and 2 (13.3%) with aortic occlusion and poor medical condition. The remaining 87 patients (85.3%) were treated with isolated anticoagulation (n=8, 9.1%), primary major amputation (n=1, 1.1%) or revascularization (n=78, 89.6%), including 69 (67.6%) embolectomies, 6 (5.9%) bypass and 3 (2.9%) endovascular techniques. Excluding palliative cases, 1-year limb salvage and survival rate was 96% and 48%, respectively. Predictive factors of lower survival included anemia (HR=1.81, p=0.014) and ALI severity (HR=1.73, p=0.032). The observed survival rate was lower than that of the general population adjusted for age, sex and year of inclusion.

Conclusion: Although nonagenarians with ALI are often functionally and cognitively impaired and have limited perspectives of survival, except in very extreme cases, most patients need revascularization for limb salvage and this can be done easily.

INTRODUCTION

Acute limb ischemia (ALI) is a limb and life-threatening vascular emergency with reported limb loss and mortality rates up to 11% and 43%, respectively (1). ALI is typically associated with certain diseases, particularly atrial fibrillation and atherosclerotic arterial occlusive disease, whose medical treatment has improved significantly over the last decades (2,3). As a result of these advances, the age of presentation of ALI in contemporary series is shifting towards elder patients (4,5).

Treatment of ALI ranges from low invasive surgical procedures, such as arterial thromboembolectomy, to more invasive interventions, such as regional fibrinolysis, often followed by an endovascular technique, and arterial bypass procedures (6-8). The consequences of a non-revascularized ALI are usually so prompt and devastating that whatever treatment has been traditionally deemed necessary, it has been done without any questioning in all but the most palliative cases.

However, as ALI cases are ageing, it is becoming frequent to encounter patients with this condition who, at the same time, are extremely frail, with cognitive impairment, bedridden or institutionalized. These characteristics are particularly frequent among nonagenarian patients (9). Unfortunately, decision-making in these patients is far from being guided by evidence. To begin, many surgeons are generally reluctant to intervene these patients by assuming that ALI may be some sort of a near-to-death condition. In addition, the few published series of nonagenarians include only intervened patients and may fail to provide the real-life spectrum of this vascular condition at these extreme ages (8-10).

The aim of our study was to describe the characteristics of a consecutive series of nonagenarian patients with an ALI attended at our institution and to determine limb salvage, survival and its predictive factors.

MATERIALS AND METHODS

We retrospectively studied the consecutive series of patients aged 90 years or more with an ALI attended in the Vascular Surgery Department of the Hospital del Mar (Barcelona, Spain), with a referral population of 330,000 inhabitants, between January 2008 and December 2021. The demographic data for our reference area reflect an approximate percentage of 1.2% of patients aged 90 years or older (11). All patients presenting with a suspected ALI at the emergency department, during any hospital admission for another reason or arriving to the outpatient clinic were immediately evaluated by the vascular surgeon on call, including only those with a diagnosis of acute ischemia after the assessment of the Vascular specialist in our study. Patients with suspected acute ischemia who were not referred to hospital or without evaluation and confirmation by a Vascular Surgeon were not included. ALI was defined as any symptomatic sudden decrease in arterial perfusion in a limb lasting less than 2 weeks. The study was carried out with the approval of the Institutional Human Research Ethics Committee (CEIC/PSMAR).

Demographic and clinical data were obtained from the electronic clinical history and the discharge sheet codes provided by our institution. In particular, dementia was considered if physician-diagnosed and categorized as advanced if required specialized care at home or institutionalization. Functional data included living (home, nursing/sheltered home, healthcare center or hospital), ambulatory (walking with or without aid, wheelchair/bedridden) and dependence status for managing one's basic physical needs

(independent or partially dependent and fully dependent). Functional information was obtained from medical and nurse records at the baseline evaluation.

Specific features of ALI included localization (upper or lower limb), etiology (embolism or acute arterial thrombosis, as determined by the attending vascular surgeon) and severity (Rutherford's classification grade I as viable ALI, IIa and IIb as threatened ALI and III as irreversible ALI) (12). Simultaneous embolism into other territories was also recorded. Prior peripheral arterial occlusive disease was considered if previously intervened or symptomatic, or when pulses in the contralateral limb were absent.

Decision-making followed several general indications shared by all the vascular team. Embolism was generally treated with thromboembolectomy regardless of the clinical severity, especially if lasting less than 3-4 days. Acute arterial thromboses were managed with the least invasive treatment possible and included anticoagulation, endovascular treatment, or bypass procedures. Intraoperative local fibrinolysis was indicated at the discretion of the operating surgeon as a complement to revascularization in patients with residual arterial thrombus. Fasciotomies were performed when compartment syndrome was present or clearly foreseen. Finally, a palliative medical approach was considered in those cases with a grade III ALI and a simultaneous cognitive impairment or malignancy, or among those with an aortic thrombotic occlusion or a simultaneous severe cerebral or visceral embolism.

Exclusions from the study included patients with an ALI secondary to the occlusion of a previous vascular procedure or those who consulted later than 2 weeks after the onset of symptoms. Recurrent episodes of ALI in the same or in another extremity were not included as new cases in the database. Primary outcomes of the study were 1-year limb salvage and survival rates. The follow-up was done by reviewing hospital and primary care records.

Categorical variables were expressed as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation. Cumulative survival and limb salvage rates were estimated according to the Kaplan-Meier method. To compare the life expectancy of our series of patients with that of the general population matched by age, sex, geographical area and year of inclusion, observed and relative survival rates were determined using the WAERS (Web Assisted Estimation of the Relative Survival) calculator (13). Cox bivariate and multivariate models were used to determine the relationship between baseline variables and 1-year survival. A $p < 0.05$ was considered statistically significant. All analyses were performed using SPSS Statistical Software (25.0 version, SPSS Inc. Chicago, IL, USA).

RESULTS

One hundred and six nonagenarians with ALI were consecutively attended at our institution during the period of study. Of these, 4 (3.7%) patients were excluded because of missing information about functional data at the beginning of the series. Among the remaining 102 patients, 80 (78.4%) were female and the mean age was 92.4 years. ALI was secondary to a native artery occlusion in the upper (20 cases, 19.6%) or lower extremity (82 cases, 80.4%). Hypertension was the most prevalent vascular risk factor (87.3%). Seventy patients (68.6%) had cognitive impairment, being advanced in 16 (15.7%). Functionally, 36 (35.3%) patients required a wheelchair to mobilize, 43 (42.2%) were totally dependent for activities of daily living, and 35 (34.5%) were institutionalized. The baseline characteristics of the patients are described in Table 1.

In 83 cases (81.4%) the ALI was attributed to an arterial embolism, whereas in the remaining 19 (18.6%) an acute arterial thrombosis (including 3 cases of a complicated popliteal aneurysm, 2.9%) was diagnosed. The limb was acutely threatened (Rutherford II) in

71 cases (69.6%) while in 9 cases (8.8%) irreversible changes were seen at presentation. Up to 43 patients (42.1%) had some degree of peripheral arterial occlusive disease (PAD), mostly asymptomatic, with only 3 cases (2.9%) of mild intermittent claudication. In 7 cases (6.9%) a simultaneous embolism in the visceral or cerebral territories was diagnosed. The characteristics of the ALI episode are detailed in Table 2.

Patients were managed as follows (see flowchart in Figure 1). A first group of 15 (14.7%) patients were considered not eligible for any specific ALI treatment and were managed with palliative care. These patients were characterized by a higher percentage of atrial fibrillation, severe dementia, wheelchair mobility, total dependence to manage basic physical needs, and living in a nursing home (Table 1). Palliative group included 8 patients with an irreversible ALI plus a severe cognitive disorder or a non-treated malignancy, 5 cases with a simultaneous severe cerebral or visceral embolism and 2 patients with a severe thrombotic aortic occlusion and poor medical condition. None of these patients survived after 10 days.

A second group of 87 patients had their ALI eligible for a non-palliative treatment at baseline evaluation. Eight patients (9.1%) were managed with anticoagulation, 78 (89.6%) with a revascularization procedure and one with a primary major amputation. Thromboembolectomy was the most frequent vascular procedure (69 cases, 67.6%), followed by bypass (6 cases, 5.9%) and endovascular (3 cases, 2.9%) techniques. 1-month and 1-year survival rates were 82.7% and 48%, respectively, whereas limb salvage at these periods was 96% in both cases. Baseline independent risk factors associated with lower survival rates included anemia (HR 1.81, p=0.014) and the severity of the ALI episode as measured by the Rutherford classification (HR 1.73, p = 0.032) (Table 3).

Among the whole population of study, 30 patients (29.4%) died within the first month after the ALI episode, 15 (50%) because a palliative approach was decided from the

beginning and 15 (50%) after a specific treatment of ALI was performed. Patients surviving 1 month after the ALI episode had a 1-year limb salvage of 95.8%, similar to the whole non-palliative group, and 1-year survival of 61.1%, significantly below that of a similar matched population (Figure 2).

DISCUSSION

Our study includes the largest series to date of nonagenarian patients with an ALI and provides important data regarding the clinical presentation and expected results in this vascular emergency at extreme ages of life. Most of our patients presented with limb threatening ischemia secondary to an arterial embolism and could be managed with limb-related success by means of a simple surgical procedure. Direct palliative care or major amputation were uncommon. Survival results, however, were not as good as limb salvage. Mortality rates were relevant at one month while, importantly, patients surviving this postoperative period had lower survival rates when compared with a general population matched by age, sex, year and location, which reveals that patients presenting with an ALI have probably underlying conditions that limit their life-expectancy.

Available data in the literature concerning ALI in nonagenarians is scarce and biased by including only patients who have undergone a reconstructive arterial surgery. Wheatley et al (5) reviewed their results in vascular surgical interventions in nonagenarians and centenarians with ALI, chronic limb threatening ischemia (CLTI), carotid stenosis, and aortic aneurysms. They concluded that it is essential to individualize treatment, taking into account comorbidities and the life expectancy of the patient, and that age per se is not a determining factor for rejecting surgery in this age group. Saarinen et al (9) evaluated nonagenarian patients with ALI and CLTI submitted to reconstructive surgery and concluded that the revascularization policy is limited by a high 1-year mortality. They observed that dementia is

an independent risk factor for mortality, so recommended conservative treatment whenever possible in these patients. Our results differed from those of Saarinen. Since embolism is the most frequent cause of ALI in nonagenarians and most times can be managed with a simple thrombo-embolectomy, we have commonly intervened patients with dementia provide no other limiting condition existed with good limb-related results. This probably would not apply to patients in which the ALI treatment requires a bypass procedure or when the advanced dementia is also associated with a very near-to-death condition, which has not been the case in our series.

Two additional clinical studies have included nonagenarian patients with ALI treated with surgical management. Galzerano et al (10) studied a limited number of patients treated with thromboembolectomy and supplemented endovascularly if necessary. They concluded that despite a significant functional limitation and high mortality, age should not constitute a criterion of exclusion for an ALI specific treatment. Finally, Dubouis et al (8) have provided the largest published series to date (83 patients) of surgically treated nonagenarians with ALI. They identified as risk factors of survival heart failure, a previous history of cerebrovascular events, the severity of ALI (paralysis) and dependency. Among our patients, the severity of ALI presentation was also associated with lower survival rates although the use of this criterion to favor a more palliative approach is problematic. It is true that a severe reperfusion can trigger the death of the patient and that such a reperfusion can be associated with the revascularization of a highly jeopardized limb. However, patients with neurological involvement are by no means more difficult to treat that many of those with a less severe ALI, and in these patients a quick salvage intervention can normalize the neurological involvement (which defines the ALI Rutherford degree) almost immediately after surgery. Similarly, our study suggests that other ‘common sense’ criteria for favoring a palliative approach such as dementia, functional limitation or dependence are not associated with

increased mortality rates and thus should be not used in clinical practice. In contrast to the few published articles in the field of Vascular Surgery, important series on the treatment of nonagenarians have been reported in other specialties, such as Cardiology (14,15), Neurology (16,17) and Orthopedic surgery (18). Published evidence globally supports that age alone must not be a limitation for intervention in these patients (19), although their life prognosis is poor and it remains an issue that has to be considered on a case by case basis (20).

The present study has several limitations that are worth to be mentioned. First, this is a retrospective study which entails the possibility of having retrieved imprecise or wrong information. In addition, this design has also impeded us to obtain confident data about nutritional status, frailty and other geriatric relevant data. Second, despite the adjusted factors found seemed clinically reasonable, these variables were subjectively selected and therefore there is a possibility that other potential risk factors were not described. Third, the number of patients included in our series, although unaffected by selection bias, is limited and results must be considered cautiously. Last, this is a single institution investigation so our results should be verified in other populations in future research.

Despite these limitations, the results of our study support a policy favoring the standard management of ALI in nonagenarian patients except in the most palliative scenarios. There is a growing general tendency to progressively involve nonagenarian patients in surgical procedures across different specialties. ALI should not be an exception. Most of these patients arrive with an acute limb threatening condition and a non-complex surgery can restore function and viability in the majority of cases, even when patient has clinical features that, at a first glance, may refrain from surgery, such as dependence or a moderate dementia. With this policy, the proportion of patients in which a palliative treatment or a direct major amputation are indicated can be kept at a minimum. Obviously, the fate of these patients is

marked by their increased risk of mortality, but at these ages, as in others, keeping the integrity of the body and avoiding amputation remains fundamental.

REFERENCES:

1. Baril DT, Ghosh K, Rosen AB (2014) Trends in the incidence, treatment, and outcomes of acute lower extremity ischemia in the United States Medicare population. J Vasc Surg 60:669e77e2.
2. Björck M, Earnshaw JJ, Acosta S, et al (2020) Editor's Choice - European Society for Vascular Surgery (ESVS) 2020 Clinical Practice Guidelines on the Management of Acute Limb Ischaemia. Eur J Vasc Endovasc Surg. 59(2):173-218. Doi: 10.1016/j.ejvs.2019.09.006.
3. Spanos K, Athanasoulas A, Argyriou C, et al (2016) Acute limb ischemia and anticoagulation in patients with history of atrial fibrillation. Int Angiol 35:510e5.
4. Seguí N, Ruiz-Carmona C, Velescu A, et al (2018) Acute Limb Ischemia Secondary to Native Artery Occlusion: Results of a Contemporary Case Series. World J Surg 42(8):2674-2681. Doi: 10.1007/s00268-018-4511-3.
5. Wheatley BJ, Gorsuch JM, Mansour MA, et al (2011) Vascular procedures in nonagenarians and centenarians are safe. Am J Surg 201(3):301-4. Doi: 10.1016/j.amjsurg.2010.09.016.
6. Berridge DC, Kessel DO, Robertson I (2013) Surgery versus thrombolysis for initial management of acute limb ischaemia. Cochrane Database Syst Rev 20(6):CD002784.
7. Amonkar SJ, Cleanthis M, Nice C, et al (2008) Outcomes of intra-arterial thrombolysis for acute limb ischemia. Angiology 58(6):734-42.
8. Dubouis A, Vernier-Mosca M, Rinckenbach S, et al (2021) Results of the Surgical Management of Acute Limb Ischemia in the Nonagenarians. Ann Vasc Surg 70:378-385. Doi: 10.1016/j.avsg.2020.05.073.

9. Saarinen E, Vuorisalo S, Kauhanen P, et al (2015) The benefit of revascularization in nonagenarians with lower limb ischemia is limited by high mortality. Eur J Vasc Endovasc Surg 49(4):420-5. Doi: 10.1016/j.ejvs.2014.12.027.
10. Galzerano G, de Donato G, Setacci F, et al (2013) Acute limb ischemia in nonagenarians. J Cardiovasc Surg (Torino) 54(5):625-31.
11. Instituto de estadística de Cataluña (2020). *Estimación poblacional por sexo y edad 2020.* Available in: http://www.idescat.cat/pub/?id=ep&n=9123&geo=prov:08&lang=es
12. Rutherford RB (2009) Clinical staging of acute limb ischemia as the basis for choice of revascularization method: when and how to intervene. Semin Vasc Surg 22(1):5-9. Doi: 10.1053/j.semvascsurg.2008.12.003.
13. WAERS: Web Assisted Estimation of the relative survival. Available in: http://regstattools.net/.
14. Liu Y, Du Y, Fu M, et al (2019) Clinical Outcomes of Transcatheter Aortic Valve Replacement in Nonagenarians: A Systematic Review and Meta-Analysis. J Interv Cardiol 24:2019:5819232.
15. Presutti DG, D'Ascenzo F, Omedè P, et al (2013) Percutaneous coronary intervention in nonagenarian: a meta-analysis of observational studies. J Cardiovasc Med 14(11):773-9.
16. Bai X, Zhang X, Zhang Y, et al (2021) Mechanical Thrombectomy in Nonagenarians: a Systematic Review and Meta-analysis. Transl Stroke Res 12(3):394-405.
17. Ospel JM, Kashani NN, Menon B, et al (2020) Endovascular Treatment Decision Making in Octogenarians and Nonagenarians: Insights from UNMASK EVT an International Multidisciplinary Study. Clin Neuroradiol 30(1):45-50.

18. Kitridis D, Tsikopoulos K, Givissis P, et al (2022) Mortality and complication rates in nonagenarians and octogenarians undergoing total hip and knee arthroplasty: a systematic review and meta-analysis. Eur Geriatr Med 13(3):725-733.
19. Noguchi M, Ueyama H, Ando T, et al (2022) Clinical outcomes in nonagenarians undergoing transcatheter aortic valve implantation: a systematic review and meta-analysis. Cardiovasc Interv Ther 37(1):202-208.
20. Thourani VH, Jensen HA, Babaliaros V, et al (2015) Outcomes in Nonagenarians Undergoing Transcatheter Aortic Valve Replacement in the PARTNER-I Trial. Ann Thorac Surg 100(3):785-92.