

# Differentiating Arteriosclerotic Ulcers of Martorell from Other Types of Leg Ulcers Based on Vascular Histomorphology

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**Clinical differential diagnosis of arteriosclerotic ulcers of Martorell is challenging due to the lack of clearly affirmative instrument-based diagnostic criteria. The aim of this study was to develop vascular histomorphological diagnostic criteria differentiating Martorell ulcers from other types of leg ulcers. The histomorphology of patients diagnosed with arteriosclerotic ulcers of Martorell (n=67) was compared with that of patients with venous leg ulcers, necrotizing leukocytoclastic vasculitis, pyoderma gangrenosum, and non-ulcerative controls (n=15 each). In a multivariable logistic regression model, the rates of arteriolar calcification (odds ratio (OR) 42.71, 95% confidence interval (CI) 7.43–443.96,  $p < 0.001$ ) and subendothelial hyalinosis (OR 29.28, 95% CI 4.88–278.21,  $p < 0.001$ ) were significantly higher in arteriosclerotic ulcers of Martorell. Arteriolar cellularity was significantly lower in Martorell ulcers than in controls (OR 0.003, 95 CI  $< 0.001$ –0.97,  $p = 0.05$ ). However, the wall-to-lumen ratio was similar in all ulcers (OR 0.975, 95% CI 0.598–2.04,  $p = 0.929$ ). Based on the Youden index, a wall cellularity of  $< 0.24$  cells/100  $\mu\text{m}^2$  was determined as the optimum cut-off point (sensitivity 0.955, specificity 0.944). Thus, arteriolar calcification, subendothelial hyalinosis, and arteriolar cellularity revealed high discriminatory power for arteriosclerotic ulcers of Martorell.**

**Key words:** arteriosclerosis; Martorell; leg ulcer; histomorphology; hyalinosis.

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The differential diagnosis of leg ulcers covers a wide range of diagnoses, often posing a difficult diagnostic challenge. Approximately 75% of all ulcers occur due to vascular aetiologies (1). While most leg ulcers are caused by chronic venous insufficiency (2), arterial disease represents the second leading cause (3). Besides peripheral arterial occlusive disease, stenotic diseases of the cutaneous arterioles are also significant. Originally described by Fernando Martorell in 1945 (4, 5), the arteriosclerotic ulcer of Martorell (ASUM) is defined

## SIGNIFICANCE

The arteriosclerotic ulcer of Martorell is characterized by necrotic leg ulcers and is associated with long-standing arterial hypertension. Differential diagnosis, however, is challenging due to a lack of clearly affirmative instrument-based diagnostic criteria. This study provides quantitative histomorphological information on arteriolar wall changes in patients with arteriosclerotic ulcer of Martorell in comparison with ulcerative and/or non-ulcerative controls. This information may facilitate the histological diagnosis, differentiating Martorell ulcers from other types of leg ulcers, and may also contribute to a better understanding of the aetiopathogenesis of the disease.

by several characteristics. These include location of the ulcer on the lower leg, absence of relevant macrovascular diseases, disproportionate pain, and longstanding arterial hypertension (4, 5). It is characterized by skin infarctions, presenting with deep necrotic ulcers and purple-reddish edges (6). Although the exact prevalence of ASUM remains to be elucidated, recent reports estimate that it accounts for up to 5% of all leg ulcers (7). Treatment with sharp necrosectomy, followed by vacuum-assisted negative pressure and split-thickness skin grafting, has achieved the most successful results, leading to remission in up to 90% of patients (7). However, the clinical differential diagnosis is challenging, given the lack of clearly affirmative instrument-based diagnostic criteria. Nevertheless, the differential diagnosis of ASUM harbours the risk of underdiagnosis or misdiagnosis. This is particularly disconcerting considering the reports of frequent misdiagnosis with necrotizing leukocytoclastic vasculitis or pyoderma gangrenosum (PG), potentially resulting in fatal complications due to immunosuppressive treatment (1, 7–10). Previously published diagnostic criteria (4, 5, 11), such as arterial hypertension or tissue necrosis, are not specific to ASUM. Thus, the criteria can only be used to stratify risk populations. In addition, considering that the patient population of ASUM consists primarily of multimorbid elderly patients, mixed ulcer aetiologies are frequent (7, 12–14). Uncovering a potential arteriosclerotic component in these cases, based simply on clinical criteria, seems impossible. Therefore, histological assessment of peri-ulcerative skin biopsies