PREDICTORS ASSOCIATED TO LOWER LIMB ULCER IN PATIENTS WITH CHRONIC RENAL FAILURE

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OBJECTIVES

Lower limb ischemia in dialysis patients is frequent and clinically relevant: this event influences quality of life, physical activity and life expectancy.
The aim of this study was to investigate risk factors associated to the **occurrence of ischemic foot ulcers (primary outcome)**, considering variables from three main domains: clinical, laboratory and therapy.

METHODS

This retrospective cohort observational study was based on data recruited from the clinical monocentric database of Nephrology and Dialysis department of Alessandro Manzoni Hospital in Lecco.
All incident patients who started dialysis between 1.1.1999 and 29.2.2012 were enrolled and followed until 15.5.2012; temporary guests, patients with acute renal failure or with previous limb ischemia or amputation were excluded.
Multivariate Cox regression analysis was performed in two steps: firstly identifying relevant covariates from each domain, and then matching them in a final model. We used time-dependent approach to take into account the evolution of some prognostic factors during the follow-up.

Covariates:

Grouped into **three domains**:
- clinical
- therapeutic
- laboratory

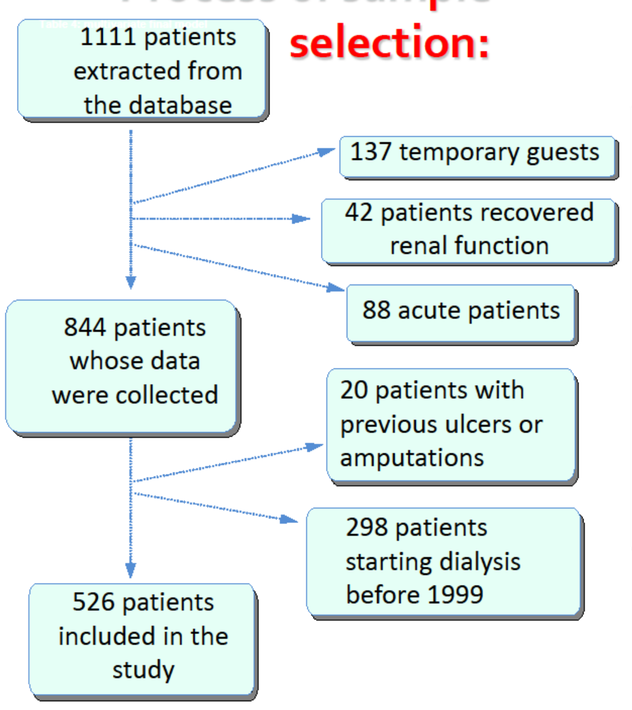
FIXED, measured at baseline
- demographic factors: age, gender
- clinical features: weight, initial dialysis type
- comorbidities: diabetes, hypertension

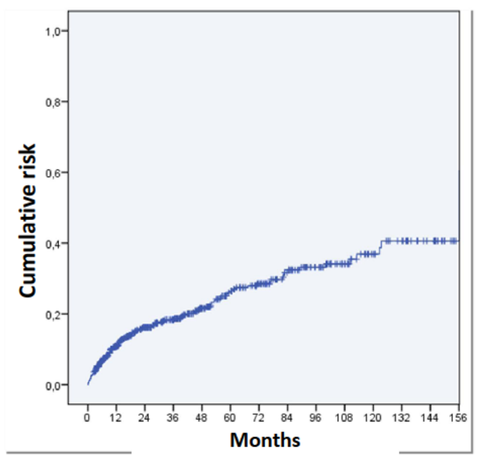
TIME-DEPENDENT, summarized monthly
- dialysis sessions: changes in weight, pressure, Uf,
- therapy: binders, iron, epo, nitroderivatives, ...
- laboratory: Ca, P, albumin, blood glucose, triglycerides

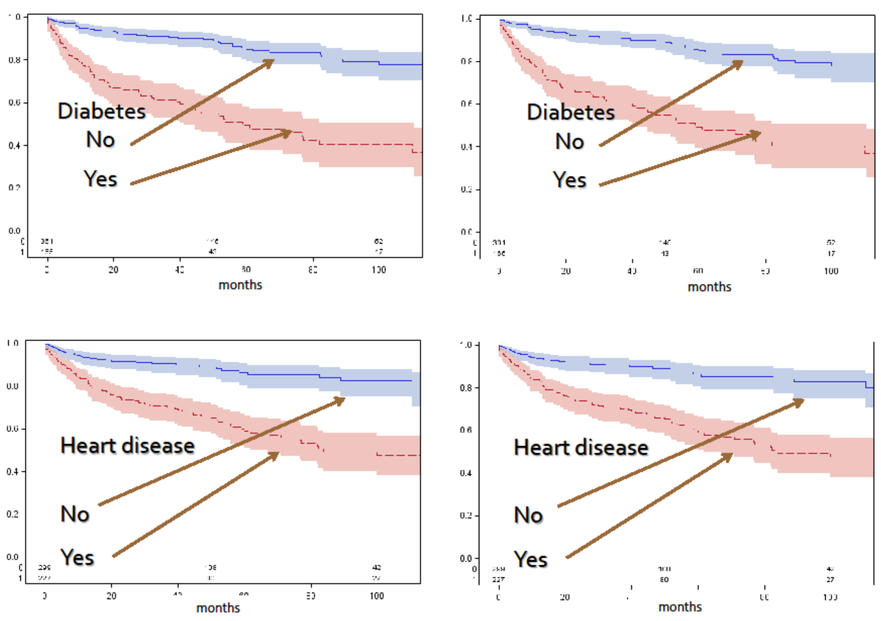
RESULTS

526 uremic patients were recruited; 120 of them developed a lower limb ischemic lesion after a median survival time of 13 months.

Process of sample selection:







Demographic and clinical characteristics of patients at baseline.

Variable		Total (n=526)	ULCER (n=120)	Not ULCER (n=406)
Gender	M	315 (59,9)	87 (72,5)	228 (56,2)
	F	211 (40,1)	33 (27,5)	178 (43,8)
Initial treatment				
hemodialysis		405 (77,0)	106 (88,3)	299 (73,6)
peritoneal dialysis		121 (23,0)	14 (11,7)	107 (26,4)
Age (years)		64.9 ± 14.5	69.3 ± 9.8	63.6 ± 15.4
Initial weight (kg)		67.7 ± 14.2	69.8 ± 14.1	67.1 ± 14.2
Hypertension		505 (96,0)	118 (98,3)	387 (95,3)
Diabetes mellitus		165 (31,4)	72 (60,0)	93 (22,9)
Stroke or TIA		81 (15,4)	31 (25,8)	50 (12,3)
Ischemic heart disease		227 (43,2)	86 (71,7)	141 (34,7)
Moderate to severe valvular disease		107 (20,3)	32 (26,7)	75 (18,5)
Abdominal aorta aneurysm or calcification		145 (27,6)	41 (34,2)	104 (25,6)
Chronic obstructive pulmonary disease		60 (11,4)	20 (16,7)	40 (9,9)
Malignancy		107 (20,3)	23 (19,2)	84 (20,7)
Cirrhosis or chronic active hepatitis		65 (12,4)	11 (9,2)	54 (13,3)
Systolic blood pressure (mmHg)		152.0 ± 20.2	156.2 ± 21.8	150.6 ± 19.5
Diastolic blood pressure (mmHg)		81.6 ± 11.5	80.5 ± 11.6	81.9 ± 11.5
Differential pressure (mmHg)		70.6 ± 16.4	75.8 ± 16.7	68.9 ± 15.9
Heart rate (beat/min)		80.6 ± 12.7	80.0 ± 13.7	80.7 ± 12.3
Ultrafiltration per hour (L/h)		0.27 ± 0.21	0.33 ± 0.22	0.24 ± 0.20

Final Model

Variable	Beta	P value	Hazard Ratio (95% CI)
Gender (M)	0.608	0.052	1.84 (0.99 - 3.39)
Age (years)	0.067	<0.001	1.07 (1.04 - 1.10)
Diabetes (0/1)	1.495	<0.001	4.46 (2.37 - 8.39)
IMA heart disease (0/1)	0.863	0.006	2.37 (1.28 - 4.39)
Weight decrease (Kg)	-0.346	0.017	0.71 (0.53 - 0.94)
Proportion HD (0/1)	1.298	0.008	3.66 (1.40 - 9.61)
C reactive protein (mg/dL)	0.086	<0.001	1.09 (1.06 - 1.12)
Phosphoraemia (mMol/L)	0.816	0.001	2.26 (1.38 - 3.70)
Triglycerides (mg/dL)	0.164	0.067	1.18 (0.99 - 1.40)
Glycaemia (mg/dL)	0.285	0.158	1.33 (0.90 - 1.98)
Insulin (0/1)	0.854	0.070	2.35 (0.93 - 5.91)
Antisecretory (0/1)	1.045	0.007	2.84 (1.34 - 6.03)
Nitroderivatives (0/1)	0.577	0.132	1.78 (0.84 - 3.78)
Calcium binders (0/1)	0.982	0.021	2.67 (1.16 - 6.17)
Calcium mimetics (0/1)	-4.871	0.012	0.01 (0.00 - 0.34)
Anticoagulants (0/1)	1.250	0.005	3.49 (1.46 - 8.36)
Iron (0/1)	1.673	0.015	5.33 (1.38 - 20.59)
Vitamin D (0/1)	-0.821	0.092	0.44 (0.17 - 1.14)

CONCLUSIONS

Incidence rate of lower limb ulcers was higher in the early follow-up.
Some modifiable predictors like calcium-based binders, phosphorus and triglycerides levels were independently associated to this phenomenon, in addition to the well-known role of diabetes.
Iron therapy could have a pathogenic role but further studies are needed to explore better this aspect.

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