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Risk Predictors of Lower-limb Amputation in Patients with Type 2 Diabetes Mellitus in the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) Study

K. Rajamani[1,*], L. Li[1], J. Best[2], M. Voysey[1], R. Ting[1], M. D'Emden[3], M. Laakso[4], J. Baker[5], A. Keech[1]

[1] *NHMRC Clinical Trials Centre, University of Sydney, Sydney, Australia*
[2] *School of Medicine, University of Melbourne, Melbourne, Australia*
[3] *Royal Brisbane and Women's Hospital, Brisbane, Australia*
[4] *Department of Medicine, University of Kuopio, Kuopio, Finland*
[5] *Middlemore Hospital, Auckland, New Zealand*

Introduction: Lower limb amputations associated with type 2 diabetes have major implications for morbidity and mortality. The aim of this analysis was to identify important risk predictors for future lower limb amputation on the basis of a large cohort of 9795 patients with type 2 diabetes mellitus in the FIELD study.

Methods: Patients were randomised to receive fenofibrate 200 mg/day or matching placebo over five years, and amputation events (a prespecified tertiary endpoint) were documented at six-monthly intervals. Time to cardiovascular disease events and death according to the predicted risk of amputation was also evaluated. Multivariable proportional-hazards regression analysis using exhaustive-search methods was used to develop predictive models.

Results: The main predictors of the first on-study amputation were a history of previous diabetic skin ulcer or nontraumatic amputation (hazard ratio (HR) 5.6), neuropathy (HR 3.0), peripheral vascular disease (HR 2.6), age over 65 years (HR 2.04) and height (HR 1.5 per 10 cm taller) (all $P < 0.001$). Other significant predictors included smoking, albuminuria, HBA1c, retinopathy and PTCA. Increasing risk of cardiovascular disease events and death was associated with increasing model-predicted amputation risk ($P < 0.0001$).

Conclusion: Classical markers of macrovascular and microvascular risk predicted amputations. We also identified height as a major predictor of diabetic amputations, independent of the presence of neuropathy, confirming a previous report from an observational study. These findings could enable more aggressive targeting of modifiable risk factors among patients at high risk of amputations and cardiovascular events who would benefit most from therapeutic intervention.

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Single-pill Combination of Telmisartan 80 mg/Amlodipine 10 mg Provides Superior Blood Pressure Reductions in Patients with Severe Hypertension: Teamsta Severe HTN Study

J. Neutel[1], G. Mancia[2], H. Black[3], B. Dahlöf[4], H. Defeo[5], L. Ley[6,*], R. Vinisko[5]

[1] *Orange County Research Center, CA, USA*
[2] *University of Milano-Bicocca, San Gerardo Hospital, Milan, Italy*
[3] *New York University School of Medicine, NY, USA*
[4] *Sahlgrenska University Hospital/Östra, Sweden*
[5] *Boehringer Ingelheim Pharmaceuticals Inc, CT, USA*
[6] *Boehringer Ingelheim GmbH & Co. KG, Ingelheim, Germany*

Purpose: Investigate the efficacy and safety of the single-pill combination of telmisartan 80 mg/amlodipine 10 mg (T80/A10) vs. its respective monotherapy components in patients with severe hypertension.

Methods: An eight-week, double-blind, parallel-group study, in 858 patients aged ≥18 years with severe hypertension (i.e. SBP ≥180 and DBP ≥95 mm Hg) randomised to T80/A10 ($n = 421$) or to monotherapy with T80 ($n = 217$) or A10 ($n = 220$). The primary endpoint was change from baseline in seated trough cuff SBP.

Results: Baseline characteristics were comparable between the treatment groups. At eight weeks, significantly greater reductions from baseline in seated trough SBP/DBP were observed with T80/A10 vs. T80 or A10 monotherapy, with superior reductions evident at one week. BP control and response rates were consistently higher with T80/A10 vs. T80 or A10 alone. T80/A10 was well tolerated, with similar rates of common adverse events (AEs) vs. T80 or A10 monotherapy. Treatment-related AEs were less frequent with T80/A10 (12.6%) vs. A10 (16.4%), with a numerically lower incidence of peripheral oedema and rate of treatment discontinuation.

	T80/A10 single-pill	T80	A10
Baseline SBP/DBP (±SD, mm Hg)	185.4 ± 4.6/103.2 ± 6.3	185.6 ± 4.5/103.5 ± 6.8	185.1 ± 4.5/103.5 ± 6.2
Adjusted mean SBP/DBP change from baseline (±SD, mm Hg)	−47.5 ± 13.3[a,b]/−18.7 ± 8.1[a,c]	−36.9 ± 16.3/−13.8 ± 8.5	−43.2 ± 12.4/−16.3 ± 7.9
SBP control (<140 mm Hg, %)	57.0	29.2	44.9
BP control (<140/<90 mm Hg, %)	50.4	35.6	24.1
SBP/DBP response (<140 mm Hg or ≥10 mm Hg decrease/DBP <90 mm Hg or ≥10 mm Hg decrease, %)	99.7/91.4	91.5/69.3	98.5/83.9

[a] $p < 0.0001$ to T80 alone.
[b] $p = 0.0002$ to A10 alone.
[c] $p = 0.0006$ to A10 alone.

Conclusions: Treatment of severe hypertensive patients with a single-pill combination containing T80/A10 results in significantly greater BP reductions (−47.5/−18.7 mm Hg) and higher BP control/response rates than the respective monotherapies. The safety pro-