

Do GLP-1 Medications Influence Lower Extremity Free Tissue Transfer Outcomes in Diabetic Limb Salvage Patients? A 13-Year Retrospective Review

Rachel N. Rohrich, BS¹; Finn Tobias BA²; Ryan P. Lin, MD¹; Sami Ferdousian, MS¹; Jayanti A. Kulkarni, MS²; Meghan E. Currin, BA².; Richard C. Youn, MD¹; Christopher E. Attinger, MD¹; Kenneth L. Fan, MD¹; Karen K. Evans, MD¹;

¹Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, Washington, DC, USA ; ²Georgetown University School of Medicine; Washington, DC, USA

Introduction

- Glucagon-Like Peptide 1 (GLP-1) receptor agonist medications are increasingly used for obesity and diabetes management.
- GLP-1 agonists are associated with a significantly reduced risk of lower extremity (LE) amputation in patients with type 2 diabetes, offering even greater risk reduction compared to other antidiabetic therapies such as SGLT-2 inhibitors.^{1,2}
- Improved cellular repair and reduction in oxidative stress through autophagy regulation in pancreatic β -cells and inflammation modulation may be benefits of GLP-1 signaling, thus promoting wound healing.^{3,4}

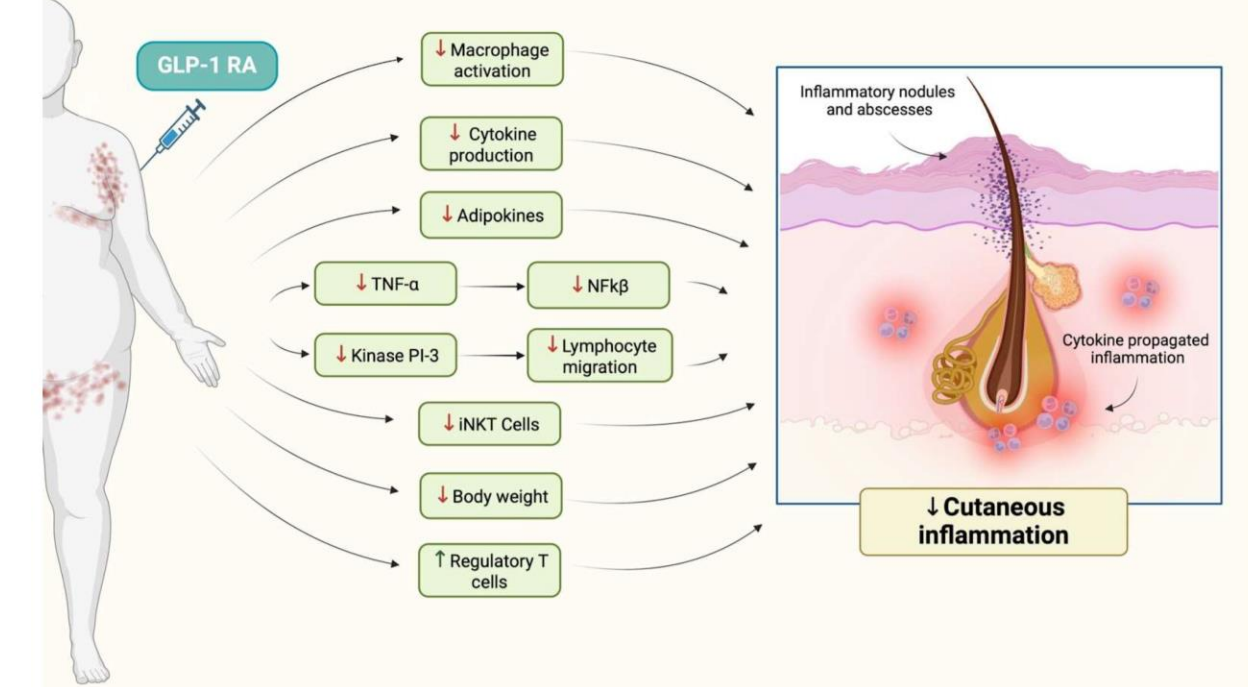


Figure 1. Possible effects of GLP-1 agonists to limit inflammation.⁵

Objective

To investigate the impact of GLP-1 medications on LE free tissue transfer (FTT) outcomes in diabetic limb salvage patients.

Methods

- A cross-sectional retrospective review of all LE FTT performed in diabetic patients from 2011 to 2024 was performed.
- Demographics, GLP-1 use, preoperative laboratory values, operative details and outcomes were collected.
- Descriptive statistics and multivariate logistic regression were performed.

Results

Patient Population

- 198 LE FTT were performed in 192 diabetic patients
- The preop GLP-1 group had higher median body mass indices (31.2, IQR: 7.4 vs. 29.3, IQR: 8.3; p=0.024).
- A shorter postop hospital stay was observed in the preop GLP-1 group (12 [12] days vs. 16 [9] days, p=0.031).
- Median A1c was similar between the GLP-1 group and controls (7.1, IQR: 2.4 vs. 7.4, IQR: 3.4; p=0.333).
- Rates of peripheral arterial disease (68.8%), neuropathy (67.2%), and chronic kidney disease (18.2%) were similar between groups.
- GLP-1 patients showed higher albumin levels (3.4 $\pm$ 0.6 g/dL vs. 3.0 $\pm$ 0.7, p=0.015) and elevated preoperative WBC (9.8 [4.0] vs. 7.8 [4.0], p=0.049).

GLP-1 Characteristics

	Control	Preop GLP-1	p-value
Total No. Patients	175 (88.4%)	23 (11.6%)	
GLP-1 Use Postop	18 (10.3%)	19 (82.6%)	<0.001*
Time from FTT to GLP-1 Use, days (median [IQR])	536.5 [1,046]	17.5 [26]	<0.001*

Surgical Outcomes

- Incidence of immediate flap success (100.0% vs. 96.7%, p=1.000), flap revision within the first 7 postoperative days (15.8% vs. 5.0%, p=0.095), and partial flap necrosis (15.8% vs. 4.5%, p=0.076) was similar between preop and postop GLP-1 and control groups
- Incidence of amputation following FTT was significantly lower (0.0% vs 11.9%, p=0.027) between preop and postop GLP-1 and control groups

Patient Demographics

	Control	Preop GLP-1	p-value
Total No. Patients	175 (88.4%)	23 (11.6%)	
Body Mass Index, kg/m ² (median [IQR])	29.3 [8.3]	31.2 [7.4]	0.024*
Age, years (mean $\pm$ SD)	58.3 $\pm$ 11.4	59.0 $\pm$ 7.1	0.754
Postop Hospital Stay, days (median [IQR])	16 [9]	12 [12]	0.031*
Hemoglobin A1c (median [IQR])	7.4 [3.4]	7.1 [2.4]	0.333
CCI (median [IQR])	5 [2]	5 [2]	0.386
Peripheral Vascular Disease	121 (69.1%)	16 (69.6%)	0.967
Chronic Kidney Disease	32 (18.3%)	5 (21.7%)	0.776
Peripheral Neuropathy	118 (67.4%)	17 (73.9%)	0.638
Preop Albumin, g/dL (mean $\pm$ SD)	3.0 $\pm$ 0.7	3.4 $\pm$ 0.6	0.015*
Preop White Blood Cell (WBC), cells/ μ L (median [IQR])	7.8 [4.0]	9.8 [4.0]	0.049*

GLP-1 Usage

- GLP-1 medication was used by 23 patients (11.6%) at time of FTT
- Median usage duration of GLP-1 was 14 months (IQR: 27.7 months)
- GLP-1 usage significantly increased over the study period (p=0.005)

Surgical Outcomes

	Control	Preop and Postop GLP-1	p-value
Total No. Patients	179 (90.4%)	19 (9.6%)	
Immediate Flap Success	173 (96.7%)	19 (100.0%)	1.000
Flap Takeback	9 (5.0%)	3 (15.8%)	0.095
Partial Flap Necrosis	8 (4.5%)	3 (15.8%)	0.076
Amputation	19 (11.9%)	0 (0.0%)	0.027*
Immediate Flap Success	173 (96.7%)	19 (100.0%)	1.000

Discussion

- On linear regression, **patients receiving GLP-1 medications had notably lower odds of amputation compared to controls**, although this difference did not reach statistical significance (OR 0.094, 95% CI: 0.006–1.59, p=0.102). This finding may be clinically meaningful, but larger studies are needed as we are currently limited by a small GLP-1 group (n=23).
 - GLP-1 patients showed higher preoperative albumin levels (p=0.015) and elevated preoperative White Blood Cell (WBC) levels (p=0.049), suggesting different metabolic and nutritional profiles
- Limitations*
- Retrospective study design – limits the ability to establish causality
 - Small GLP-1 cohort size
 - Cost of GLP-1 medications – potentially skews the GLP-1 cohort to include patients with more resources and access to care
 - Unknown adherence to GLP-1 medication use

Conclusion

These preliminary data suggest that GLP-1 medication may have a positive benefit on long-term limb salvage outcomes among diabetic patients with chronic LE wounds. The continued rise in GLP-1 usage warrants further prospective investigation.

References

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