



# Impact of Perioperative Hyperglycemia in Free Flap Surgery

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## Abstract

### Objective

To investigate the effect of perioperative hyperglycemia on the complication rate and free flap outcomes for patients undergoing microvascular reconstruction.

### Study Design

Single Institution Case Series

### Setting

Academic Medical Center

### Subjects and Methods

A retrospective chart review was performed on 203 consecutive patients undergoing microvascular reconstruction. Perioperative blood glucose levels and other clinical factors were tested for associations with post-operative complications, length of hospitalization, and readmission rates using simple and multivariate analyses.

### Results

Of 203 patients, 91 (44.8%) had documented perioperative hyperglycemia (blood glucose  $\geq 180$ mg/dL). On univariate analyses perioperative hyperglycemia was associated with increased surgical complications (47.3% vs 28.6%,  $p=0.006$ ), medical complications (18.7% vs 8.9%,  $p=0.042$ ), surgical site infections {SSI} (37.4% vs 17.9%,  $p=0.002$ ), fistulas (11.0% vs 2.7%  $p=0.021$ ), and wound dehiscence (26.4% vs 13.4%,  $p=0.020$ ). On univariate analysis, a more strict definition of hyperglycemia (blood glucose  $\geq 165$ mg/dL), was significantly associated with increased rates of venous thrombosis (14.0% vs 4.1%,  $p=0.026$ ), although this narrowly lost significance on multivariate analysis (Odds Ratio= 3.5,  $p=0.055$ ). Additionally, the rates of SSI and venous thrombosis increased in a dose dependent fashion with the maximum recorded blood glucose.

### Conclusion

Perioperative hyperglycemia occurs commonly and is associated with higher rates of surgical complications, SSI, and venous thrombosis that occurred independent of a pre-existing diagnosis of diabetes mellitus. The degree of hyperglycemia was associated with increasing rates of SSI and venous thrombosis in a dose dependent manner. Further research is needed to define the ideal glycemic targets in this population.

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## Introduction

Microvascular reconstruction has become a standard tool for the reconstruction of complex head and neck defects. There is extensive literature investigating the risk factors for free flap complications; however, no one has examined the impact of perioperative hyperglycemia on outcomes of patients undergoing microvascular reconstruction.<sup>1-3</sup> However, a substantial body of literature demonstrates a clear association between hyperglycemia in hospitalized patients and increased morbidity and mortality that occurs regardless of a diagnosis of diabetes prior to hospitalization.<sup>4</sup> Animal models have shown this association as well<sup>5</sup>. The aim of this study was to investigate the difference in postoperative complications and free flap outcomes in patients with perioperative hyperglycemia. Our hypotheses were that patients with perioperative hyperglycemia will have higher rates of medical and surgical complications as well as a longer hospital stay.

## Subjects and Methods

We designed a retrospective review of patients undergoing microvascular free tissue transfer for head and neck reconstruction at the University of Missouri Hospital and Clinics from July 2009 to October 2015. Patient demographics, co-morbidities, prior cancer treatment and operative details were obtained. Blood glucose (BG) levels were recorded and patients were then stratified into two groups based on whether or not they had a BG  $\geq 180$  mg/dL during the first 96 hours postoperatively. The length of hospital stay, 30-day readmission rate, and surgical re-exploration rate were collected. The rates of overall and individual medical and surgical complications were recorded. Univariate associations between glycemic status and other clinical factors were tested for associations with post-operative complications, surgical re-explorations, length of hospital stay, and 30 day readmission rates using the t-test for continuous variables and the chi-square or fisher exact test for categorical variables. Different degrees of hyperglycemia were tested for associations with vascular thrombosis. Multivariate logistic regression analysis was then performed for venous thrombosis using variables found to be significant ( $p < 0.05$ ) or nearly significant ( $p < 0.10$ ) on univariate analysis. To investigate the association between degrees of hyperglycemia and rates of SSI and venous thrombosis, we divided patients into 3 groups based on their maximum blood glucose level ( $< 165$ mg/dL,  $165 < x < 200$ mg/dL, and  $> 200$ mg/dL). For all tests, the threshold for statistical significance was set at  $p < 0.05$ .

## Results

Table 1- Patient Characteristics and Operative Details

	Total n= 203	Patients with BG < 180 n=112	Patients with BG $\geq 180$ n= 91	p value
Sex				0.532
Male, %	145 (71.4)	82 (73.2)	63 (69.2)	
Female, %	58 (28.6)	30 (26.8)	28 (30.8)	
Age				
Mean Age, y (SD)	60.3 (13.0)	57.6 (13.2)	63.5 (12.1)	*0.001
Race				0.604
White, %	194 (95.6)	106 (94.6)	88 (96.7)	
Comorbidities				
ASA 4/5, %	58 (28.6)	29 (25.9)	29 (31.9)	0.349
Prior Radiation Therapy, %	93 (45.8)	56 (50.0)	37 (40.7)	0.184
Prior Chemotherapy, %	52 (25.6)	35 (31.3)	17 (18.7)	*0.041
Diabetes Mellitus, %	25 (12.3)	1 (0.9)	24 (26.4)	*<0.001
Vascular Disease, %	50 (24.6)	22 (19.6)	28 (30.8)	0.067
Current Smoker, %	162 (79.8)	94 (83.9)	68 (74.7)	0.104
Current EtOH use, %	77 (37.9)	45 (40.2)	32 (35.2)	0.464
Intraoperative Details				
Intraop steroids, %	127 (62.6)	65 (58.0)	62 (68.1)	0.139
Blood Transfusion, %	84 (41.4)	46 (41.1)	38 (41.8)	0.921
Pressor Usage, %	148 (72.9)	82 (73.2)	66 (72.5)	0.913
Mean Operative Time, h (SD)	8.1 (1.9)	8.0 (2.0)	8.3 (1.7)	0.370
Mean Ischemic Time, min (SD)	63.7 (30.2) n=158	63.8 (29.5) n=90	63.6 (29.6) n=68	0.959
Indication				0.968
Cancer resection, %	172 (84.7)	95 (84.8)	77 (84.6)	
Recipient Site				0.335
Oral Cavity, %	121 (59.6)	60 (53.6)	61 (67.0)	
Pharynx, %	58 (28.6)	37 (33.0)	21 (23.1)	
Skin, %	16 (7.9)	11 (9.8)	5 (5.5)	
Other, %	8 (3.9)	4 (3.6)	4 (4.4)	
Flap Type				
Osteocutaneous, %	69 (34.0)	28 (25.0)	41 (45.1)	*0.003
OCRRF, %	50 (24.6)	19 (17.0)	31 (34.1)	
FFF, %	19 (9.4)	9 (8.0)	10 (11.0)	
RFFF/UFFF, %	126 (62.1)	81 (72.3)	45 (49.5)	
Latissimus/Rectus, %	8 (3.9)	3 (2.7)	5 (5.5)	
Postoperative Medications				
Postop steroids, %	99 (48.8)	47 (42.0)	52 (57.1)	*0.031
Aspirin, %	146 (71.9)	79 (70.5)	67 (73.6)	0.626

Bolded font and \* indicates a statistically significant variable.

Abbreviations: BG, blood glucose; y, years; SD, standard deviation; ASA, American Society of Anesthesiologists; h, hours; min; minutes; OCRRF, osteocutaneous radial forearm free flap; FFF, fibular free flap; RFFF, fasciocutaneous radial forearm free flap; UFFF, fasciocutaneous ulnar forearm free flap

## Results

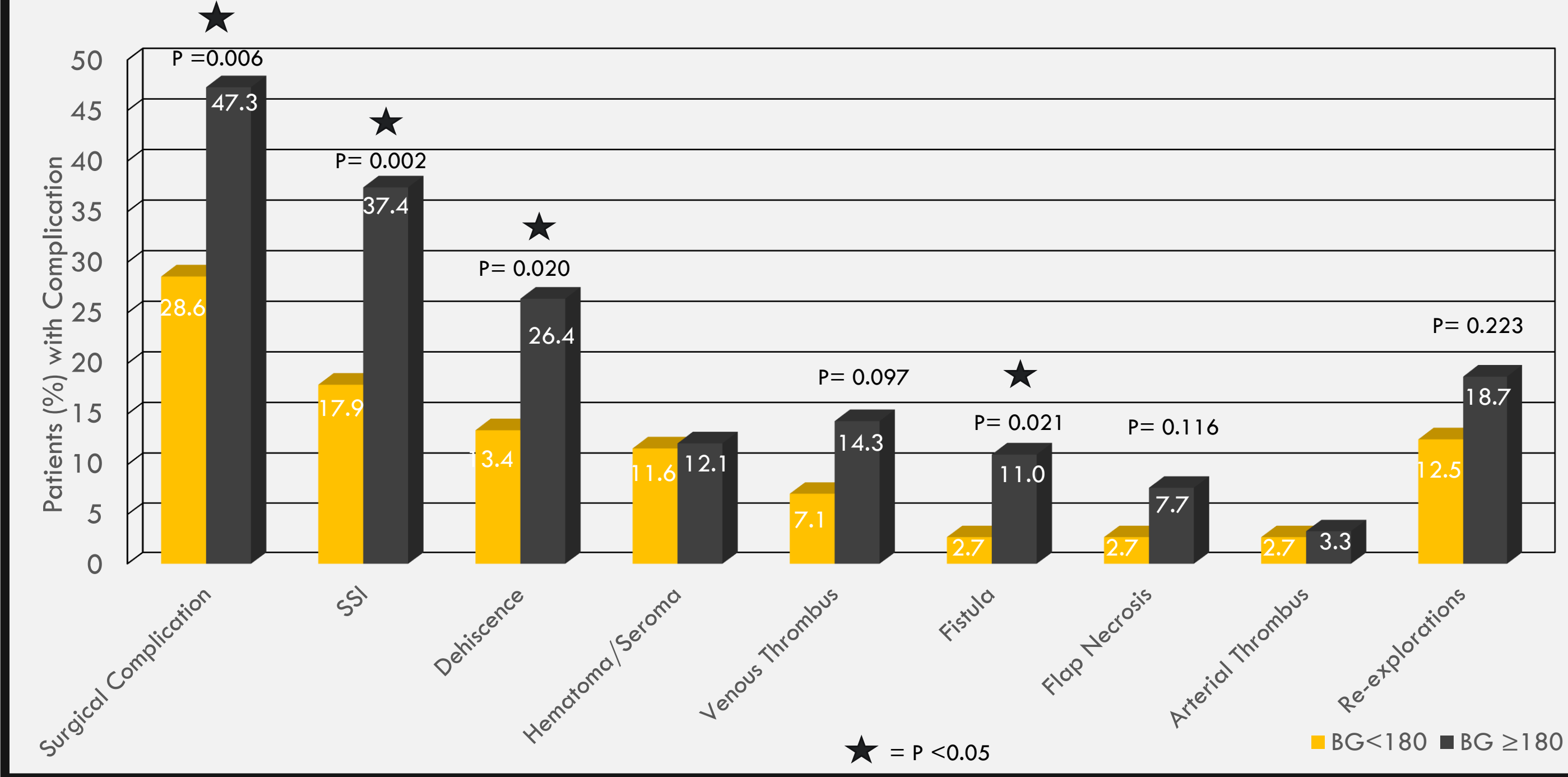
Table 2 - Medical Complications, Re-admission Rates, and Length of Hospitalization

	Total n= 203	Patients with BG < 180 n=112	Patients with BG $\geq 180$ n=91	p value
30-Day Readmissions, n (%)	22 (10.8)	10 (8.9)	12 (13.2)	0.332
Mean Hospital Stay Length, d (SD)	9.8 (5.7)	9.3 (4.6)	10.4 (6.7)	0.415
Patients with complication, n (%)	27 (13.3)	10 (8.9)	17 (18.7)	*0.042
Myocardial Infarction, n (%)	3 (1.5)	1 (0.9)	2 (2.2)	NT
Pneumonia, n (%)	9 (4.4)	4 (3.6)	5 (5.5)	NT
CVA, n (%)	2 (1.0)	0	2 (2.2)	NT
Meningitis, n (%)	1 (0.5)	0	1 (1.1)	NT
Death, n (%)	1 (1.0)	0	2 (2.2)	NT
Other, n (%)	10 (4.9)	5 (4.5)	5 (5.5)	NT

Bolded font and \* indicates a statistically significant variable.

Abbreviations: BG, blood glucose; y, years; SD, standard deviation; CVA, cerebrovascular accident

Figure 1 Surgical Complications & Re-explorations



★ indicates a statistically significant variable.

Abbreviations: SSI, Surgical Site Infection; BG, Blood Glucose

Table 3. Summary Univariate Analysis of Factors Significantly Associated with Surgical Complications, SSI, and Venous Thrombosis.

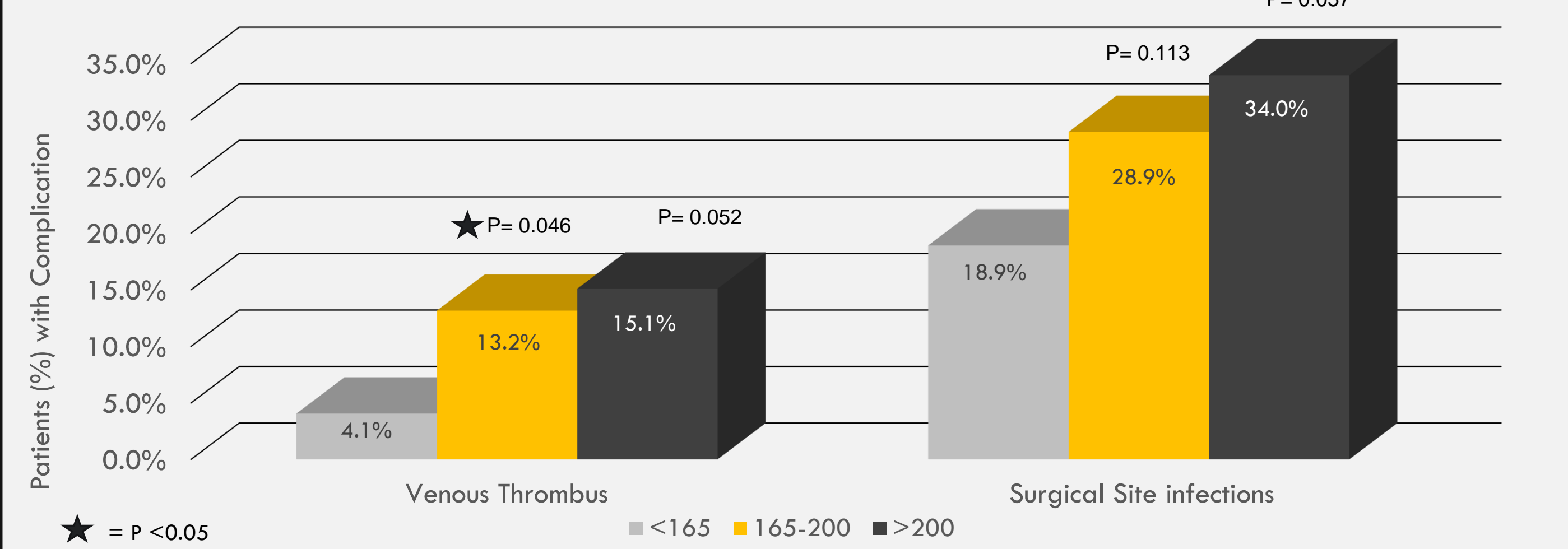
Variable	Surgical Complications	SSI	Venous Thrombosis
Age	No	No	No
ASA Class 4 or 5	No^	No	Yes*
Aspirin	No	No	No
Blood Glucose $\geq 180$	Yes*	Yes*	No^
Blood Glucose $\geq 165$	Yes*	No^	Yes*
Bone Flap	No	No	No
Chemotherapy	No	No	No
Diabetes Mellitus	No	No	No
Vasopressors	No	No	No
Radiation Therapy	No	No^	No^
Recipient Site	No	No	No
Tobacco Use	No	No	No
Vascular Disease	No	No^	No

Bolded font and \* indicate a statistically significant variable

^ indicates a nearly statistically significant variable (p value between 0.05 and 0.1)

Abbreviations: BG, blood glucose; y, years; SD, standard deviation; ASA, American Society of Anesthesiologists;

Figure 2 Association of Venous Thrombosis and SSI with Maximum Blood Glucose Level (mg/dL)



★ indicates a statistically significant variable.

Abbreviations: SSI, Surgical Site Infection

Table 4 Multivariate Analysis of Risk Factors for Venous Thrombosis

Variable	Adjusted Odds Ratio	95% Confidence Limits	p value
Blood Glucose $\geq 165$ mg/dL	3.5	0.97	12.46
ASA 4/5	2.6	0.99	6.75
Radiation Therapy	0.4	0.14	1.055

Abbreviations: ASA, American Society of Anesthesiologists

## Discussion

Similar to those in prior reports, patients in our review with perioperative hyperglycemia consistently experienced more frequent complications and worse outcomes independent of a pre-existing diagnosis of diabetes mellitus, although some of these outcomes did not reach statistical significance.

Likely the most important outcomes of interest to surgeons are vascular thrombosis and flap necrosis. In our patient cohort, there were clinically meaningful differences in the rates of venous thrombosis and flap necrosis when using our initial definition of hyperglycemia that approached, but did not reach statistical significance. However, a lower threshold of 165 mg/dL demonstrated a significant association with venous thrombosis on univariate analysis and approached statistical significance on multivariate analysis. In accordance with prior reports, rates of complications increased in a dose-dependent fashion with glucose levels.<sup>6</sup>

This review provides the first description of the detrimental effects associated with perioperative hyperglycemia in patients undergoing microvascular reconstruction. It highlights the importance of glycemic control in this population. Furthermore, given the dose-dependent relationship between maximum glucose levels and rates of SSI and venous thrombosis, it may provide evidence for tighter control than is currently used. Because patients undergoing microvascular reconstruction are already intensely monitored post-operatively for flap viability, they may be a surgical population that is appropriate for using more intensive glycemic targets ( $< 140$ mg/dL).

## Conclusions

In our retrospective review perioperative hyperglycemia occurred commonly and was associated with greater rates of overall surgical complications, surgical site infections, and venous thrombosis that occurred independent of a pre-existing diagnosis of diabetes mellitus. The degree of hyperglycemia was associated with increasing rates of SSI and venous thrombosis. Further research is needed to define the ideal glycemic targets in this population.

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