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Difference between Capillary Blood Glucose of Free Flap and the Patient: A Novel Objective Marker of Free Flap Vascular Compromise during Postoperative Monitoring

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Abstract

Background Defining cut-off values of flap glucose levels in diagnosing free flap vascular compromise, without taking patients' glucose levels into account, does not hold good in all circumstances, especially in cases of high fluctuations in patients' capillary blood glucose and in diabetic patients. The aim of our study was to establish the role of capillary blood glucose measurements of the flap in relation to patients' fingertip, as an objective tool for postoperative free flap monitoring.

Methods A total of 76 free flaps underwent postoperative monitoring with reference test (clinical parameters) and simultaneously with our index test (difference between capillary blood glucose of free flap and the patient), in non-diabetic and diabetic patients. Patients' demography and flap characteristics were also recorded. An ROC curve was plotted to determine diagnostic accuracy and cut-offs of the index test in diagnosing free flap vascular compromise.

Results Our Index test has a cut-off value of 24.5 mg/dL with 68.75% sensitivity and 93% specificity, with an accuracy of 91.54%.

Conclusion The difference between capillary blood glucose of free flap and the patient is simple, feasible, and inexpensive, and can be done by any health care professional and does not require any specialized facilities or training. It has an excellent diagnostic accuracy to detect impending free flap vascular compromise,

Keywords
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- capillary glucose measurement
- objective monitoring

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especially in non-diabetics. Although in diabetics, this test becomes less accurate. Being an observer-independent objective test, the difference in capillary blood glucose of patient and flap measurement can be used as a highly reliable tool for postoperative free flap monitoring.

Introduction

Free flap glucose monitoring is the cheapest and the most readily available tool among all the techniques of postoperative free flap monitoring, objectively. However, the horizon of capillary sugar monitoring as a standard test for free flap monitoring has been limited due to two reasons. Firstly, after extensive literature search, we found that in all those studies evaluating free flap blood glucose levels for postoperative monitoring,[1–5] diabetic patients have always been excluded. Secondly, the glucose levels of study patients were also not recorded in the postoperative period. It has been shown that the blood glucose concentration within flap decreases under ischemic or congestive condition,[6] using the microdialysis system. But its' relationship with patients' blood glucose levels, which also fluctuate in immediate postoperative period especially in an ICU setting, has not been explored so far.

In this study, we explored a novel measurement as an index test (difference between capillary blood glucose of patient's fingertip and reconstructed free flap) for postoperative free flap monitoring, and standardized the cut-off values to be used as an objective tool to diagnose impending flap failure by even less-experienced healthcare providers in a resource-or a trained manpower-constrained healthcare set-up. Our primary objective was to estimate the diagnostic accuracy (sensitivity and specificity) of the index test in determining free flap vascular compromise during postoperative free flap monitoring. Our secondary objective was to determine the difference in the diagnostic accuracy of the index test for postoperative free flap monitoring among non-diabetic and diabetic (controlled/uncontrolled) patients.

Methods

This was a diagnostic accuracy cross-sectional study. All patients were consecutively sampled who underwent free flap reconstruction from September 2019 to December 2021.

Operational Definition

The difference between capillary blood glucose of patient's fingertip and reconstructed free flap is referred as the Index test. The gold standard test to monitor free flap postoperatively (i.e., clinical examination)[7] is referred as the Reference test. The inclusion criteria for the study were based on PICOT framework-participants, intervention, reference standard used for comparison, and outcomes (►**Table 1**). All patients who underwent free fasciocutaneous/musculocutaneous/ muscle flap reconstruction for any defect (post-traumatic/-post-excision of neoplastic lesion/burn contracture) were included. Written informed consent was taken from all patients for participation in the study.

Data Collection

Free flap monitoring was done immediately after operation, postoperatively at 2, 4, 6, 12, 24 hours and then single time on postoperative days 2, 3, and 4 as applicable. Clinical parameters including, flap color, temperature, turgor, and bleeding pattern of surface scratch were employed for flap monitoring. Simultaneously, flap blood was sampled after scratching the surface with a 26-G needle and measuring the flap capillary blood glucose (CBG) levels using SD Code free glucometer (SD Code free; SD Biosensor Inc., Gyeonggi-do, South Korea). Patients' fingertip CBG was also measured using the same instrument. All sterile precautions were maintained. Final diagnosis of

Table 1 PICOT design

Criteria	Description
P-Participant	Patients who underwent free fasciocutaneous/musculocutaneous/muscle flap reconstruction for any defect (post traumatic/post excision of neoplastic lesion). No restriction on participant age or gender or demographic characteristic or any co-morbidity (e.g., diabetes) was used.
I-Index test	Difference between capillary blood glucose of patients' fingertip and reconstructed free flap
C-Comparison (Reference test)	Clinical examination (Color, temperature, turgor, bleeding pattern on scratch test)
O-Outcomes	Diagnostic accuracy (sensitivity and specificity) of Index test for postoperative free flap monitoring.
T-Time	Four postoperative day (primary reconstruction or revision surgery, whichever is later)

flap congestion or ischemia, if any, was made by the same senior author according to clinical examination, as described by Mathes[8] to minimize any inter-observer bias. Another author monitored the flap and patients' blood glucose values. As far as possible, they were mutually blinded of other's findings. In case of an impending flap failure, the flap was re-explored and managed accordingly. Following the re-exploration. flap monitoring was done immediately after operation, and at 2, 4, 6, 12, 24 hours and subsequently, similar to previous explanation. Occurrence of complications (complete or partial necrosis, infection, suture line dehiscence, hematoma/seroma/abscess collection, free flap failure) was recorded. In cases where free flap could not be salvaged and reconstruction was done with another free flap, then again, the same flap monitoring protocol was followed. Possible variables related to the results such as age of patient, gender, co-morbidities (diabetes), defect site and etiology, and donor free flap were also recorded. The study was conducted according to the ethical guidelines laid down by declaration of Helsinki, and institutional ethical clearance was taken.

Statistical Analysis

The participants' data were entered into Microsoft Excel 2016 sheet and exported into SPSS (Statistical Package for the Social Sciences) software VERSION 23 (IBM, Armonk, NY, USA). Descriptive measures are presented in tabular form with percentage for discrete variables (flap characteristics) and mean value with standard deviation (capillary glucose levels in flap). Receiver operating characteristic (ROC) curve was plotted using the MedCalc statistical software[9] to determine the cut-off value to diagnose free flap vascular compromise, and sensitivity and specificity were reported with 95% confidence Interval.

Results

A total of 70 patients were enrolled, majority being male patients (►**Table 2**). Nineteen patients were diabetics. More than half of the patients underwent free flap reconstruction for malignant condition, free fibula flap being the most commonly used donor flap. Double free flap reconstruction was done in four patients. A total of 532 capillary blood glucose readings (532 each for flaps and patients' fingertip) were taken. Ten free flaps underwent complete necrosis and could not be salvaged due to extensive thrombosis (►**Table 2**). In two of these patients subsequently, another free flap reconstruction was successfully done, while in six patients, pedicled or local flap was done. Among these flap failure patients, one patient died in the immediate postoperative period. Three flaps were salvaged on exploration following flap congestion (salvage rate 23%). The index test has excellent discriminating power to diagnose impending flap failure, in any type of patients [Area under the curve = 0.816; 95% CI: 0.713, 0.919; p = 0.000] (►**Fig. 1**). The ROC curve determined a cut-off value for difference in CBG (patient's flaps) of 24.50 mg/dL, at which the sensitivity and specificity were 68.75% [95% CI: 49.99% to 83.88%] and 93% [95% CI: 90.40% to 95.08%] (p < 0.000), respectively (►**Table 3**). The various cut-offs of the index test (difference in patient's and flap's CBG), with their sensitivities and specificities are mentioned in ►**Table 4**. The diagnostic accuracy of the index test is excellent among the non-diabetic patients [area under the curve = 0.934; 95% CI: 0.864, 1; p = 0.000] (►**Fig. 2**). The ROC curve determined a cut-off value for difference in CBG of 31.5 mg/dL, at which the sensitivity and specificity were 84.21% [95% CI: 60.42% to 96.62%] and 96.4% [95% CI: 93.79% to 98.12%], respectively (►**Table 5**). However, the test has poor discriminating power among the diabetic patients to differentiate between compromised and normal free flaps [area under the curve = 0.656; 95% CI: 0.473, 0.840; p = 0.039] (►**Fig. 3**). The ROC curve determined a cut-off value for difference in CBG of 24.5 mg/dL, at which the sensitivity and specificity were 50% [95% CI: 24.65% to 75.35%] and 93.9% [95% CI: 89.07% to 97.04%] (►**Table 5**).

Table 2 Patients' demographics and flap characteristics

Age, mean (range)*	43.67 years (13–75)
Gender*	
Male	58 (82.8%)
Female	12 (17.1%)
Comorbid with diabetes*	
Yes	19 (27.1%)
No	51 (72.8%)
Flap indication**	
Trauma	21 (27.6%)
Malignancy	42 (55.2%)
Post burn sequelae	4 (5.3%)
Others	3 (3.9%)
Flap types**	
Free anterolateral thigh flap (ALT)	24 (31.6%)
Free medial sural artery perforator flap (MSAP)	5 (6.6%)
Free LD	9 (11.8%)
Free fibula	27 (35.5%)
Free gracilis	1 (1.3%)
Free parascapular	1 (1.3%)
Free radial artery forearm flap (RAFF)	9 (11.8%)
Complications**	
Total flap failure	10 (13.1%)
Venous congestion that was relieved	3 (3.9%)
Arterial ischemia	1 (1.3%)
Hematoma evacuation	1 (1.3%)
Distal part necrosis	3 (3.9%)
Death	1 (1.3%)

*Total number of patients is 70.
**Total number of flaps is 76.

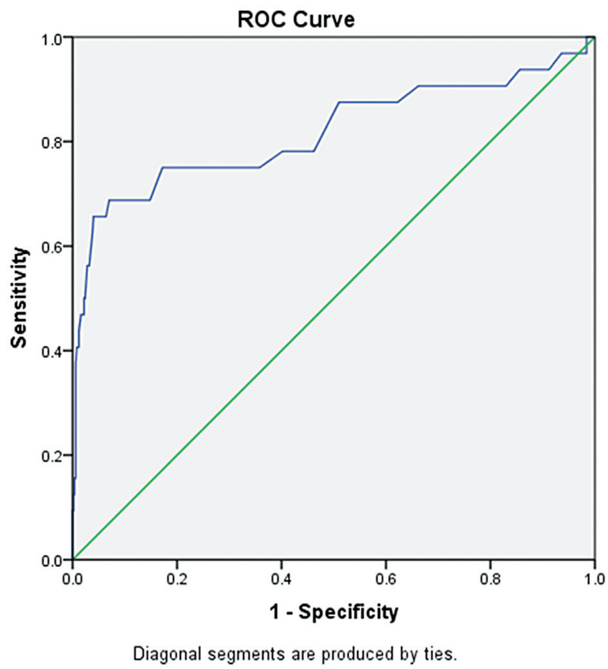

Fig. 1 ROC curve of Index test in overall patients.

Case 1

An 18-year-old non-diabetic male patient underwent free anterolateral thigh (ALT) flap reconstruction, harvested from the left thigh, for post traumatic defect (12 × 7 cm approx.) over dorsum of the right foot, with exposed extensor tendons. Recipient vessels (anterior tibial vessels) and the anastomosis were functional. Splintage was given, and the vitals and hydration of the patient were strictly monitored. Flap monitoring was done clinically immediately after operation at 2, 4, 6, 12, 24 hours and on postoperative day 2. The flap was clinically viable (no signs of ischemia or congestion), and the difference between CBG of the patient and the flap

Table 3 Overall diagnostic accuracy of the Index test

Parameters All values are with 95% CI	Difference in CBG [Patient–flap]
Cut off value	24.50
AUC	0.816 [0.713 to 0.919]
Sig	0.000
Sensitivity	68.75% [49.99% to 83.88%]
Specificity	93.00% [90.40% to 95.08%]
Positive likelihood ratio	9.82 [6.61 to 14.59]
Negative likelihood ratio	0.34 [0.20 to 0.56]
Positive predictive value	38.60% [29.73% to 48.29%]
Negative predictive value	97.89% [96.53% to 98.73%]
Accuracy	91.54% [88.85% to 93.76%]

Abbreviation: CBG, capillary blood glucose.

Table 4 Various cut-offs of the Index test and their sensitivities and specificities in overall patients

Positive if greater than or equal to[a]	Sensitivity	1-Specificity	Specificity
15.50	0.750	0.212	0.788
16.50	0.750	0.172	0.828
17.50	0.688	0.148	0.852
18.50	0.688	0.134	0.866
19.50	0.688	0.124	0.876
20.50	0.688	0.104	0.896
21.50	0.688	0.090	0.910
22.50	0.688	0.076	0.924
23.50	0.688	0.074	0.926
24.50	0.688	0.070	0.930
25.50	0.656	0.064	0.936
26.50	0.656	0.054	0.946
27.50	0.656	0.048	0.952
28.50	0.656	0.044	0.956
29.50	0.656	0.042	0.958
30.50	0.656	0.040	0.960
31.50	0.625	0.038	0.962
32.50	0.563	0.032	0.968
33.50	0.563	0.028	0.972
34.50	0.500	0.024	0.976
35.50	0.500	0.022	0.978

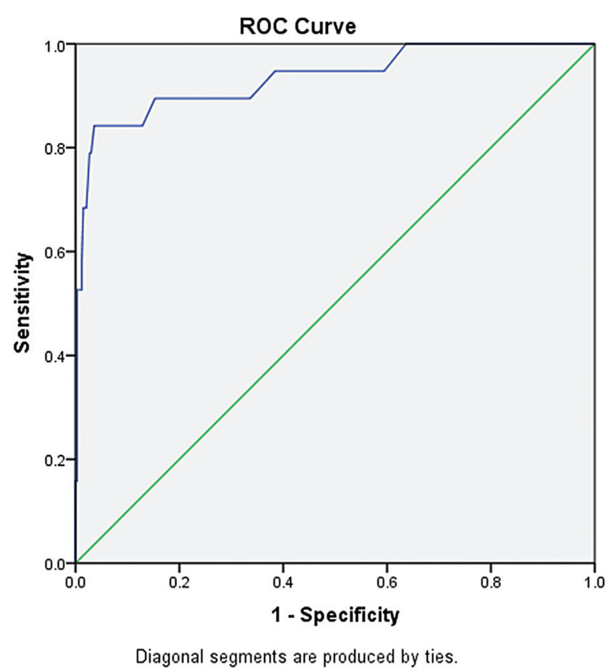

Fig. 2 ROC curve of Index test in nondiabetic patients.

Table 5 Diagnostic accuracy of the Index test in diagnosing impending flap failure among nondiabetic versus diabetic patients

Parameters [All values are with 95% CI]	Difference in CBG [Patient–flap] in non-diabetics	Difference in CBG [Patient–flap] in diabetics
Cut off value	31.50	24.5
AUC	0.934 (0.864 to 1)	0.656 [0.473 to 0.840]
Sig	0.000	0.039
Sensitivity	84.21% (60.42% to 96.62%)	50.00% (24.65% to 75.35%)
Specificity	96.40% (93.79% to 98.12%)	93.90% (89.07% to 97.04%)
Positive likelihood ratio	23.37 (12.97 to 42.10)	8.20 (3.78 to 17.80)
Negative likelihood ratio	0.16 (0.06 to 0.46)	0.53 (0.33 to 0.87)
Positive predictive value	57.14% (42.53% to 70.61%)	44.44% (26.93% to 63.46%)
Negative predictive value	99.07% (97.43% to 99.67%)	95.06% (92.17% to 96.92%)
Accuracy	95.74% (93.07% to 97.60%)	90.00% (84.66% to 93.96%)

Abbreviation: CBG, capillary blood glucose.

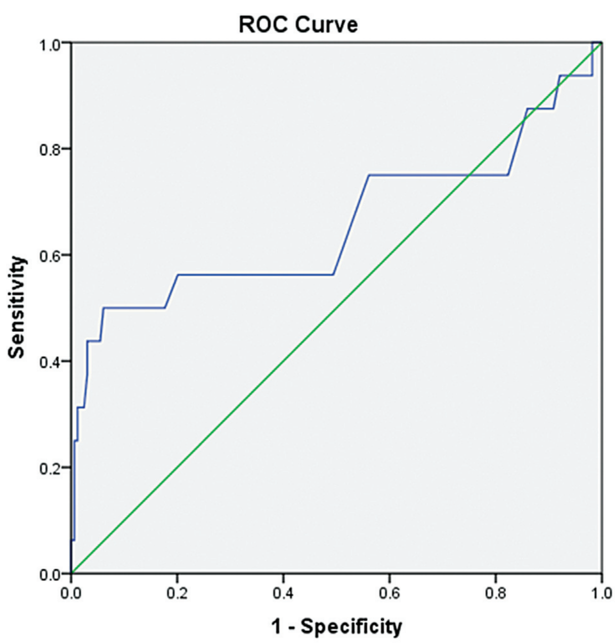

Fig. 3 ROC curve of Index test in diabetic patients.

was lower than 24.5 mg/dL in each of these instances. However, on POD 3, dark brisk bleeding was present on surface scratch and the difference in CBG was 63 mg/dL. Immediate re-exploration was planned, venous thrombosis was present. Venous anastomosis was revised, clots were removed, and the flap was salvaged (►**Fig. 4**). The flap subsequently healed well.

Discussion

Sakakibara et al[1] were first to report the use of glucometer as a monitoring tool for flap perfusion in clinical cases and also proposed that lower blood glucose indicates flap hypoperfusion. In their study on 127 flaps, Bashir et al[2] reported a cut-off value of 62 mg/dL for within flap blood glucose level, at which the sensitivity and specificity were 90% and 78%, respectively, to diagnose venous compromise. The overall diagnostic accuracy of flap blood glucose measurement for postoperative flap monitoring was 87%. Hara et al, keeping a cut-off value of 62 mg/dL, obtained a sensitivity and specificity of 88% and 82%, respectively ($p < 0.0001$), for flap blood glucose.[3] In another study by Sharma et al, using an ROC curve, the cut-off value for flap capillary sugar level was 61 mg/dL, with a sensitivity of 93% and a specificity of 80%.[4] However, all these studies evaluated the CBG for free flap, as well as of pedicled flap and estimated the cut-off values as combined results. In an attempt to obtain more accurate monitoring method for flap congestion Karakawa et al[5] measured the ratio of blood glucose level change (RBGC) within the free flap in 36 free tissue transfers. They reported that the mean RBGCs at points in time when the venous thrombosis was detected was −7.61 mg/dL h and those at times when the flap demonstrated no venous thrombosis was 0.10 mg/dL h, the former being significantly lower than the latter.

In all previous studies, patients' CBG was never considered for cut-off value calculation. It is noteworthy that in both poorly and well-perfused free flap, the glucose level of the flap is deemed to be affected by the patient's glucose levels. In the immediate postoperative period, in ICU settings, we observed that patients' glucose levels fluctuate, especially in head and neck reconstruction cases. This fluctuation accentuates in diabetic patients. Even in well-perfused free flaps, the CBG levels change significantly over the course of 48 hours postoperatively in stable patients.[10]

Our study results demonstrate that the index test (difference in the CBG of patient and free flap) has an excellent diagnostic accuracy in diagnosing an impending free flap failure. The cut-off value in overall patients is 24.5 mg/dL. Among non-diabetic patients, the sensitivity and specificity of the test are the highest, and cut-off value to diagnose any vascular compromise of the flap was 31.5 mg/dL. However,

Fig. 4 (**A**) Capillary blood glucose of free flap at POD 0. (**B**) Capillary blood glucose of fingertip at POD 0. (**C**) Capillary blood glucose of free flap at POD 3. (**D**) Capillary blood glucose of fingertip on POD 3. (**E**) Thrombosed anastomotic veins with mildly congested flap on exploration on POD 3. (**F**) Final salvaged free flap.

the sensitivity and specificity of this test decreased among diabetic patients. This might be due to large fluctuations in glucose levels of the patient and at times, very high values of glucose (especially in uncontrolled diabetes mellitus) in the postoperative period. The cut-off value of the test as determined by the ROC curve among diabetics was 24.5 mg/dL.

The measurement of difference in the CBG of patients and flap is simple and can be performed by residents, nurses, and patients themselves using simply a glucometer. The primary advantage of this test is that it does not require the expertise as required for clinical examination. It is also useful for monitoring intraoral free flaps, which are difficult to monitor on the basis of flap color. The depth of the scratch is up to the dermal layer and has no adverse effect on the vascularity of the flap.

However, there are certain limitations with this measurement too. Firstly, we could not explain the fact that there were a few readings in which the flap glucose was more than the patient's CBG. Secondly, using this test, we cannot monitor the buried free flaps or if the amount of blood sample withdrawn was inadequate for testing. This test alone could not differentiate venous congestion from arterial insufficiency in free flap failures. Larger sample size with proper randomization could produce more uniform cut-off values. Confounding factors such as delay between the two scheduled readings might affect the cut-off values. Lastly, there was unequal number of diabetic and non-diabetic patients.

Conclusively, we can propose that the difference in CBG measurement (patients versus free flap) might possibly be a useful, easy, and accessible parameter to monitor free flap postoperatively. Any value more than 24.5 mg/dL is suggestive of vascular compromise within the free flap, with sensitivity and specificity of 68.75% and 93%, respectively (accuracy of 91.54%), and thus, warrants re-exploration. Although it cannot outweigh the clinical judgement of diagnosing an impending free flap vascular compromise by an experienced eye, as it is difficult to set an exact cut-off value in all circumstances, this simple and reliable measurement can be used as an objective tool for monitoring the free flap postoperatively, especially for an inexperienced observer in a resource- or a trained manpower-constrained healthcare set-up.

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None.

Conflict of Interest
None declared.

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