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Original Article

Reliability of Early Detection of Venous Flap Congestion by Measuring Blood Glucose Level in Albino Rat; Experimental Study

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ABSTRACT:

Background: Nowadays, flap surgery is a dependable reconstructive technique. It makes it possible to heal nearly any vascularized tissue defect in the body. The present work aimed to assess the effectiveness of flap blood glucose measurement as a sensitive and reliable indicator in early detection of venous congestion.

Methods: In an experimental study, twenty-six adult male Sprague-Dawley rats were subjected to vertical rectus abdominis muscle flaps with upper pedicles, were split into two equal groups (n=13): with venous occlusion of the pedicle (Cases group) and without (Control group). Between the beginning and end of the experiment, we monitored the rats' glycemia in the caudal vein of their feet at regular intervals of ten minutes, and we measured the interstitial glucose in the flaps every ten minutes.

Results: Statistically significant decrease was revealed at 0 min, 20 min, and 30 min of flap glucose level when compared with 0 min, 20 min, 30 min foot glucose level (p=0.01, p=0.005, p=0.002 respectively), and high statistically significant decrease was revealed at 10 min, 40 min, 50 min, 1-hour of flap glucose level when compared with 10 min foot glucose level (p-value < 0.001). High statistically significant decrease was found (p-value < 0.001) of mean flap glucose level (mean = 179.7 ± 54.3, range = 89.7 – 297.2) when compared with mean foot glucose level (mean = 228.1 ± 65.1, range = 114.7 – 342.1) in Cases group. Using ROC curve, it was shown that mean glucose level can be used to discriminate between flap glucose level and foot glucose level in cases group at a cutoff level of 187.2, with 69.2% sensitivity, 69.2% specificity, 69.2% PPV and 69.2% NPV (AUC = 0.7 & p-value = 0.054).

Conclusions: Monitoring blood glucose levels may serve as a promising indicator for detecting venous congestion in tissue flaps, offering a non-invasive and cost-effective approach for early intervention.

Keywords: Early Detection; Venous Flap; Congestion; Blood Glucose Level; Albino rat.

INTRODUCTION

Reconstructive flap surgery has developed into a dependable technique. Almost anywhere there is vascularized tissue on the body, it can fix abnormalities caused by surgery or trauma [1]. A prevalent reason for flap failure is the presence of venous congestion during regional and free tissue transfers [2]. Ischemia from arterial thrombosis is less prevalent and less detrimental to the flap than congestion from venous thrombosis, which is well documented [3].

One of the many causes of this problem is the veins' intrinsic anatomy, which leaves them open to damage from things like pressure or shock due to their delicate structure and thin walls. Conditions such as pedicle torsion, local edema, venous spasm, venous thrombosis, venous lack of repair, and so on [4].

Because venous insufficiency's microcirculatory changes are permanent, it's important to diagnose and treat the condition as soon as possible [5]. This is because the rate of flap salvage decreases with increasing time between the complication's occurrence and detection [6].

Traditional techniques of monitoring flaps include taking a look at their color, temperature, turgor, capillary refill, skin scratch test, pinprick/ultrasonic Doppler, and overall health after surgery to determine the flap's vascular perfusion. Clinical knowledge is necessary for interpreting the results [7,8].

Clinical cases of congestive flaps were associated with a decreased blood glucose level, according to Sakakibara et al. [9]. The optimal threshold value for detecting venous thrombosis was found to be 62 mg/dl, with a sensitivity of 88% and a specificity of 82%, according to Hara et al. [10], who detailed blood glucose testing for flap monitoring. One easy, quick, and inexpensive way to predict microvascular problems and decrease flap failure is to monitor capillary glucose levels in flaps with a glucometer [11].

Recent research aimed to assess if flab blood glucose could serve as specific as well as sensitive indicator of flab venous congestion. So, we aimed at this study to assess the effectiveness of flap blood glucose measurement as a sensitive and reliable indicator for early detection of venous congestion at the Zagazig University Hand and Microsurgery Center (ZUHMC), Plastic and Reconstructive Surgery Department.

METHODS

This experimental study was conducted on 26 Sprague-Dawley young adult male rats with an average weight of 250-350 grams. During the study period between January 2023 till March 2024; the Institutional animal care and Use committee of the Faculty of Medicine, Zagazig University, approved the study (ZU-IACUC/3/F/15/2023). Following the recommendations of the Declarations of Helsinki as well as the European Community's rules for the use of experimental animals, the experiment was carried out.

All the maneuvers carried on in this experiment concerning the rats were highly ethical and merciful. Anesthesia was administered via an intra-peritoneal injection of a Ketamine / Xylazine cocktail (Ketamine 25mg + Xylazine10mg per mL) with a dosage of 0.1 mL/100-gram rat weight then preparing the rats by shaving the abdomen.

In Group (1) Intervention (n=13): After shaving their abdomens and marking the vertical Rectus Abdominis Muscle Flap (VRAM), the rats were placed in a supine position. Using thermal plates, we positioned the rats in dorsal decubitus and executed abdominal trichotomy. The VRAM flap was dissected (fig 1 A, B). In rats, the rectus abdominis muscle's dominant pedicle, the superior epigastric vessels, were the only ones to pediculate the flap. To prevent heat loss and visceral dryness, a plastic field was placed over the abdominal cavity. Utilizing microsurgical tools and operating under four-time magnification, we carefully separated the pedicle that houses the upper epigastric veins. We punctured a vein in the back of the flap to measure the interstitial glucose every 10 minutes from the beginning (before clamping and dividing the superior epigastric vein) to the end (60 minutes). We additionally monitored the rats' caudal vein in the foot for glycemia at the same intervals. We used the MediSense Optimum glucose monitor to measure blood sugar levels (fig 1C, D).

We ended the experiment with euthanasia by administering a lethal dose of isoflurane, which can cause cardiac arrest, followed by exsanguination. Regarding the ethical considerations that pertain to animal experimentation, we adhered to all biosafety standards.

For the control group 2 (n=13); we did the same steps but we didn't ligate the vein of the flap pedicle Then we measured the flap blood glucose level every 10 minutes comparing to the Rat's caudal vein Statistical analysis was carried out using a model of generalized estimating equation25. The study involved comparing measurement times and groups (congestive flap, control flap, and systemic control), as well as the interaction between these terms.

Glycemic readings were presented as the mean plus or minus the standard deviation. We performed diagnostic analysis using cutoff thresholds determined by the Receiver Operating Characteristic (ROC) curve. In this case, we determined the sensitivity and specificity values together with the 95% CIs for both.

Statistical Analysis:

Statistical analysis was done using SPSS version 28 (IBM Co., Armonk, NY, USA). Quantitative parametric data were presented as mean, SD, and range. Categorical variables were presented as frequency and percentage (%) and analyzed using the Chi-square test or independent t-test; a P-value < 0.05 was considered statistically significant.

RESULTS

Statistically significant decrease was revealed at 0 min, 20 min, and 30 min of flap glucose level when compared with 0 min, 20 min, 30 min foot glucose level (p=0.01, p=0.005, p=0.002 respectively), and high statistically significant decrease was revealed at 10 min, 40 min, 50 min, 1-hour of flap glucose level when compared with 10 min foot glucose level (p-value < 0.001) among Cases group (Table 1).

High statistically significant decrease was found (p-value < 0.001) of mean flap glucose level (mean = 179.7 ± 54.3, range = 89.7 – 297.2) when compared with mean foot glucose level (mean = 228.1 ± 65.1, range = 114.7 – 342.1) in Cases group (Table 2).

Using ROC curve, it was shown that mean glucose level can be used to discriminate between flap glucose level and foot glucose level in cases group at a cutoff level of 187.2, with 69.2% sensitivity, 69.2% specificity, 69.2% PPV and 69.2% NPV (AUC = 0.7 & p-value = 0.054) (Table 3, Figure 2).

Statistically significant decrease also was revealed at 30 min, 40 min, 50 min, and 1 hour of flap glucose level when compared with 30 min, 40 min, 50 min, and 1 hour foot glucose level (p=0.001, p=0.001, p=0.007, p=0.001 respectively), and high statistically significant decrease was revealed at 0 min, 10 min, 20 min of flap glucose level when compared with 0 min, 10 min, 20 min foot glucose level (p-value < 0.001) among Control group (Table 4).

Table (1): comparison of glucose level between foot and flap in Cases group.

Cases group		Foot (N = 13)	Flap (N = 13)	t	P-value
Zero	**Mean ±SD**	224.8 ± 37.4	184.7 ± 47.9	**3.06**	**0.01 S**
	Range	178 -289	109 -270		
10 min	**Mean ±SD**	230.9 ± 56.4	189.8 ± 60.2	**4.8**	**< 0.001 HS**
	Range	120 -327	97 -315		
20 min	**Mean ±SD**	231 ± 70.9	186.3 ± 54.3	**3.4**	**0.005 S**
	Range	125 -366	109 -310		
30 min	**Mean ±SD**	228 ± 78.1	178.5 ± 52.7	**3.9**	**0.002 S**
	Range	109 -384	103 -291		
40 min	**Mean ±SD**	232.8 ± 80.1	180.9 ± 64.1	**5.3**	**< 0.001 HS**
	Range	102 -399	75 -306		
50 min	**Mean ±SD**	229.2 ± 82.4	175.5 ± 68.2	**5.7**	**< 0.001 HS**
	Range	75 -389	55 -299		
1 hour	**Mean ±SD**	219.6 ± 75.4	162.5 ± 64.5	**6.7**	**< 0.001 HS**
	Range	94 -337	50 -302		

S: p-value < 0.05 is considered non-significant. t: paired sample T test.
HS: p-value < 0.001 is considered highly significant.

Table (2): comparison of mean glucose level between foot and flap in Cases group.

Cases group		Foot (N = 13)	Flap (N = 13)	t	P-value
Mean glucose level	**Mean ±SD**	228.1 ± 65.1	179.7 ± 54.3	**6.3**	**< 0.001 HS**
	Range	114.7 - 342.1	89.7 – 297.2		

t: paired sample T test. HS: p-value < 0.001 is considered highly significant.

Table (3): Diagnostic performance of mean glucose level in cases group.

	Cut off	AUC	Sensitivity	Specificity	PPV	NPV	p-value
Mean glucose level	**< 187.2**	**0.7**	**69.2%**	**69.2%**	**69.2%**	**69.2%**	**0.054**

PPV: positive predictive value. AUC: Area under curve
NPV: negative predictive value.

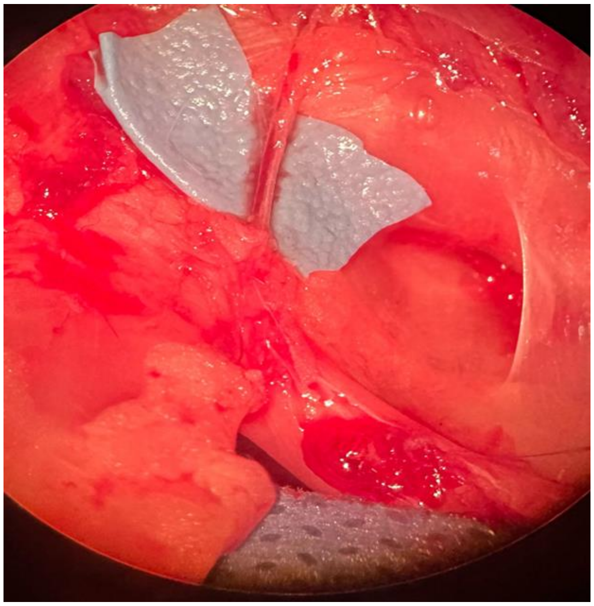
Table (4): comparison of glucose level between foot and flap in Control group.

Control group		Foot (N = 13)	Flap (N = 13)	T	P-value
Zero	**Mean ±SD**	220.5 ± 34.6	213.6 ± 32.7	**6.9**	**< 0.001 HS**
	Range	172 -287	168 -276		
10 min	**Mean ±SD**	212.6 ± 32.4	205.5 ± 32.2	**8.4**	**< 0.001 HS**
	Range	166 -269	159 -260		
20 min	**Mean ±SD**	205.6 ± 31	198.8 ± 29.7	**801**	**< 0.001 HS**
	Range	159 -250	153 -238		
30 min	**Mean ±SD**	200.4 ± 31.9	191.7 ± 28.8	**4.4**	**0.001 S**
	Range	151 -255	148 -230		
40 min	**Mean ±SD**	195.6 ± 31.8	186.5 ± 29.8	**4.2**	**0.001 S**
	Range	145 -245	142 -232		
50 min	**Mean ±SD**	191.4 ± 32.7	182.8 ± 28.3	**3.2**	**0.007 S**
	Range	140 -240	137 -220		
1 hour	**Mean ±SD**	188.2 ± 32.9	182.8 ± 27.1	**4.5**	**0.001 S**
	Range	135 -236	142 -218		

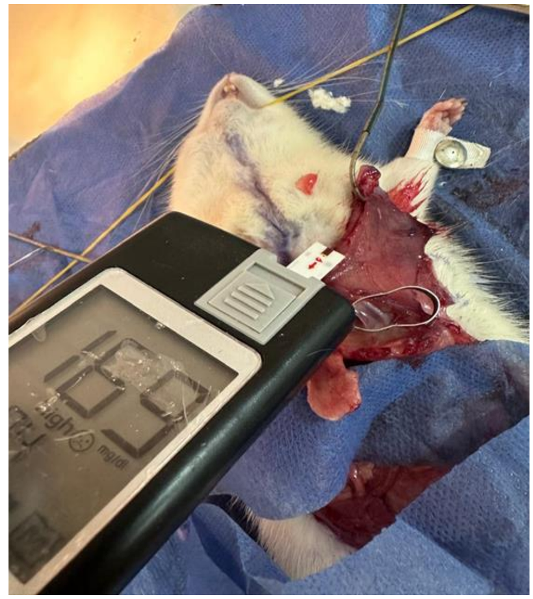
S: p-value < 0.05 is considered non-significant.
T: Independent sample T test.
HS: p-value < 0.001 is considered highly significant.

(A)

(B)



(C)



(D)

Figure 1: A) placing the rats in dorsal decubitus on thermal plates and performing abdominal trichotomy, B) dissection of the VRAM flap and pediculation of the flab, C) dissection of the pedicle containing the upper epigastric vessels, D) measurement of interstitial glucose in the flaps

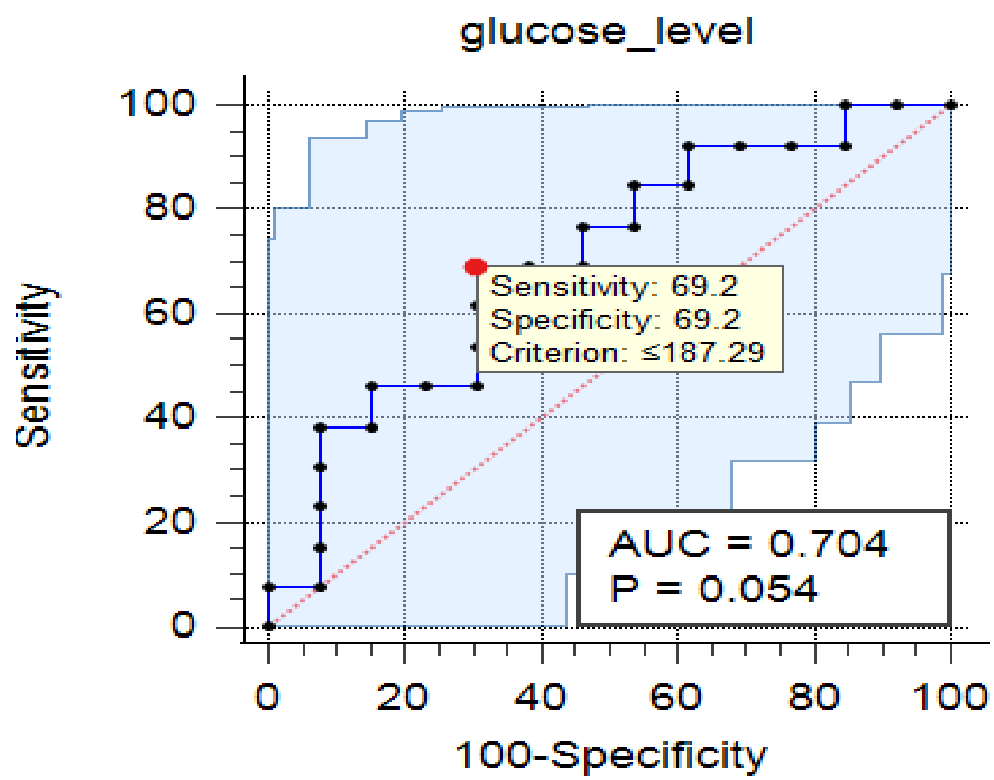


Figure 2: ROC curve between Foot and Flap in Cases group as regard mean glucose level.

DISCUSSION

The aim of that study was to assess the effectiveness of flap blood glucose measurement as a sensitive and reliable indicator in early detection of venous congestion.

The current study showed non-significant differences in foot blood glucose levels between the Cases and Control groups at zero minutes, 10 minutes, 20 minutes, 30 minutes, 40 minutes, 50 minutes, and 1 hour. The mean blood glucose ranges were the same for both groups. Also, non-significant differences were found in foot blood glucose levels at 40 minutes, 50 minutes, or 1 hour between the Cases and Control groups. The results suggested that the study does not provide a clear indication of the difference in glucose levels between the groups.

In agreement with the current study Mochizuki et al. [12] revealed that Extremely low levels of glucose in the blood were quickly achieved. The duration it took for the flap blood glucose to drop to an off-scale low following venous blockage was not significantly different between the two groups (p = 0.379). Flap blood glucose levels reverted to systemic levels within 15 minutes or less after venous declamping in both groups.

Also, Hara et al. [10] stated that when early venous thrombosis was present, blood glucose levels were low. Before flap discoloration ever happened, low capillary blood glucose levels were already discovered.

In the present study, the mean zero-minute blood glucose range was 194.7 ± 47.9 in the Cases group, while the mean 10-minute blood glucose range was 189.8 ± 60.2 in the Control group. The mean 20-minute blood glucose range was 186.3 ± 54.3 in the Cases group, while the mean 30-minute blood glucose range was 178.5 ± 52.7 in the Cases group. The mean 40-minute blood glucose range was 180.9 ± 64.1 in the Cases group, and 186.5 ± 29.8 in the Control group. The mean 50-minute blood glucose range was 175.5 ± 68.2 in the Cases group, and 182.8 ± 28.3 in the Control group. The mean 1-hour blood glucose range was 219.6 ± 75.4 in the Cases group, and 188.2 ± 32.9 in the Control group. The study concluded that flap blood glucose levels were not significantly different between the two groups at different times and locations.

In agreement with the current study findings, Mochizuki et al. [12] showed that comparing the blood glucose levels in the hyperglycemic rats with venous obstruction at each time point to those in the systemic blood, they revealed that At 10 minutes post-vein clamping, the two values quickly separated, and at 5 minutes post-declamping, the flap blood glucose level had recovered to the systemic value (p > 0.05 at 55, 60, 65, and 70 minutes).

Also, Mochizuki et al. [12] **s**tated that In terms of how long it took for the flap blood glucose level to decline below 20 mg/dl following vein clamping, there was no statistically significant difference between the two groups (flap congestion groups with and without glucose preloading; p = 0.379), Nonetheless, after declamping, the hyperglycemic rat group returned to systemic blood glucose levels substantially faster than the normoglycemic rat group (p = 0.028). There was no detrimental effect of systemic blood glucose levels on flap glucose levels, which represent the flap venous system.

As well, Choudhary et al. [11] employed a Medtronic glucometer, which is standard equipment for taking capillary blood glucose readings, to track the flaps' progress. Only little volumes of blood (10-20 μL) are needed for the quick and easy process. Along with being more quantitative, this method replaces more conventional methods of monitoring flaps, such as looking at their color, turgor, or using the pinprick test. It enables objective comparisons between experiments and serves as a surrogate reflection of the sufficiency of flap perfusion.

The current study showed Statistically significant decrease was revealed at 0 min, 20 min, and 30 min of flap glucose level when compared with 0 min, 20 min, 30 min foot glucose level (p=0.01, p=0.005, p=0.002 respectively), and high statistically significant decrease was revealed at 10 min, 40 min, 50 min, 1-hour of flap glucose level when compared with 10 min foot glucose level (p-value < 0.001) among Cases group. These findings suggested that the use of glucose monitoring devices could help in monitoring glucose levels in patients.

In the same line, Berlim et al. [13] reported that The glucose levels recorded in the congested flap decreased significantly beginning at 15 minutes after venous blockage. By utilizing a glycemic difference of at least 20mg/dl between the flap and systemic blood 30 minutes after occlusion as a diagnostic criterion, the sensitivity for the diagnosis of flap congestion was 100% (95% CI 83.99-100%) and the specificity was 90% (95% CI 69.90-97.21%).

Also, Berlim et al. [13] stated that Throughout the experiment, all animals maintained consistent systemic glucose levels. Following venous blockage, glucose levels dropped sharply in the experimental group but stayed the same in the control group. The intervention group's flaps had substantially lower glucose levels compared to the control and systemic blood groups beginning fifteen minutes following venous occlusion.

Anwar et al. [14] showed that the flap blood glucose approach was easy enough for patients, nurses, and residents to do, and it works even on intraoral flaps which were notoriously difficult to monitor using only color or temperature as indicators. Because enough blood cannot be drawn to measure the glucose level, it cannot be utilized for ischemia flaps or buried flaps, which are two of its drawbacks. Flap blood glucose may also react erratically to venous congestion in diabetic patients due to their unstable blood glucose levels, poor cellular glucose uptake, and metabolic abnormalities.

In the current study using ROC curve, it was shown that mean glucose level can be used to discriminate between flap glucose level and foot glucose level in cases group at a cutoff level of 187.2, with 69.2% sensitivity, 69.2% specificity, 69.2% PPV and 69.2% NPV (AUC = 0.7 & p-value = 0.054). High statistically significant (p-value < 0.001) decreased mean flap glucose level (mean = 179.7 ± 54.3, range = 89.7 – 297.2) when compared with mean foot glucose level (mean = 228.1 ± 65.1, range = 114.7 – 342.1) in Cases group.

The present study findings were in accordance with Berlim et al. [13] who reported that diagnostic criteria for flap congestion that took comparative glucose levels into account were more precise than those that relied solely on glycemic levels. The sensitivity and specificity values, as well as the area under the curve (ROC) for the comparison criteria, show that they are more precise.

Free flaps were assessed in 37 individuals by Henault et al. [15]. Hypoperfusion and tissue glucose and lactate levels were assessed with threshold values of 69.37 mg/dL and 57.66 mg/dL, respectively. They achieved a sensitivity of 98.5% and a specificity of 99.5% using these criteria, and the clinical examination helped them diagnose hypoperfusion about 5.4 hours before the actual diagnosis.

In their work, Akita et al. [16] compared the levels of glucose and tissue oximetry in flaps. They utilized indices that compared values recorded in the flaps to those recorded in a different, non-operated area of the body for both checks. Each assessment was useful in that research, however tissue oximetry allowed for a quicker diagnosis.

According to Hara et al. [10], who detailed the use of blood glucose monitoring for flap monitoring, the optimal cutoff value for detecting venous thrombosis is 62 mg/dl, with a sensitivity of 88% and a specificity of 82%.

A lower flap blood glucose concentration was hypothesized by Sakakibara et al. [9] as a result of the continuous intake of glucose from stagnant blood for tissue metabolism in venous thrombosis.

Ischemia is associated with a decrease in blood glucose levels, as demonstrated in multiple studies; this decrease is both more rapid and more broad than the decrease seen in patients with congestion. Also, compared to congestion, ischemia causes a more dramatic and quick increase in lactate concentration. It appears from these results that decreased blood glucose in ischemia and congestion is caused by a combination of a lack of glucose supply and an increase in anaerobic respiration in the tissues.

Flaps with vascular problems showed a drop in blood glucose, according to Sakakibara et al. [9], proving that the glucose checker's sensitivity is enough to detect venous complications.

Nonetheless, the method has not yet been tested on uncompromised free flaps; thus, its specificity is unknown.

CONCLUSIONS

The experimental study examining the reliability of early detection of venous flap congestion by measuring blood glucose levels in albino rats provides valuable insights into potential diagnostic methods for assessing flap viability. The findings suggest that monitoring blood glucose levels may serve as a promising indicator for detecting venous congestion in tissue flaps, offering a non-invasive and cost-effective approach for early intervention.

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