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Article

PREDICTING FREE FLAP VIABILITY: INTEGRATING LACTATE AND GLUCOSE MEASUREMENTS WITH ARTIFICIAL INTELLIGENCE

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ABSTRACT

Introduction: In reconstructive surgery, free flaps are a superior method for resurfacing defects. While free flap viability is typically monitored by subjective clinical examination, lactate and glucose levels in free flaps, which can affect tissue metabolism during ischaemia and reperfusion, can help predict viability. This study aims to review previous research and provide a theoretical basis for using artificial intelligence in lactate and glucose measurement as a means of assessing flap viability.
Method: The primary databases used to retrieve the key medical literature presented in this study were book references and Google Scholar, PubMed and Science Direct, using search terms related to the topic. Only articles written in English and published less than ten years ago were included.
Results: Lactate levels detect perfusion impairment earlier than clinical signs or other biochemical markers while glucose monitoring can indicate underlying metabolic dysregulation or physiological stress, helps early detection of complications. Combining lactate and glucose measurements enhances diagnostic accuracy and allows for timely interventions for flap viability. Studies confirm this dual monitoring is a practical, unbiased, and has the potential to be developed into an artificial intelligence tool to improve patient outcomes.
Conclusion: Lactate and glucose measurements in free flap monitoring have distinct benefits. Lactate detects ischaemia and reflects tissue metabolism, while glucose monitors energy metabolism and systemic health. Combining these leading to improved flap survival rates. With accessible tools, this approach improves patient care and outcomes in reconstructive surgery.

Key Words: *Free flap monitoring; Lactate; Glucose; Tissue metabolism; Artificial intelligence.*

Pendahuluan: Dalam bedah rekonstruktif, free flap merupakan metode unggul untuk menutup defek jaringan. Meskipun viabilitas free flap umumnya dipantau melalui pemeriksaan klinis subjektif, kadar laktat dan glukosa dalam free flap, yang berperan dalam metabolisme jaringan selama iskemia dan reperfusi, dapat membantu memprediksi viabilitas jaringan. Studi ini bertujuan untuk meninjau penelitian sebelumnya dan memberikan dasar teoretis bagi penggunaan kecerdasan buatan (artificial intelligence/AI) dalam pengukuran laktat dan glukosa sebagai metode asesmen viabilitas free flap.
Metode: Basis data utama yang digunakan untuk memperoleh literatur medis dalam penelitian ini meliputi referensi buku serta Google Scholar, PubMed, dan ScienceDirect, dengan kata kunci terkait topik ini. Artikel yang dimasukkan dalam studi ini hanya yang ditulis dalam bahasa Inggris dan diterbitkan dalam kurun waktu kurang dari sepuluh tahun terakhir.
Hasil: Kadar laktat dapat mendeteksi gangguan perfusi lebih awal dibandingkan tanda klinis atau biomarker biokimia lainnya, sedangkan pemantauan glukosa dapat menunjukkan adanya disfungsi metabolik atau stres fisiologis, sehingga membantu deteksi dini komplikasi. Kombinasi pengukuran laktat dan glukosa meningkatkan akurasi diagnosis dan memungkinkan intervensi tepat waktu untuk mempertahankan viabilitas free flap. Studi menunjukkan bahwa pemantauan ganda ini bersifat praktis, objektif, serta memiliki potensi untuk dikembangkan menjadi alat berbasis kecerdasan buatan guna meningkatkan luaran klinis pasien.

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Kesimpulan: Pengukuran laktat dan glukosa dalam pemantauan free flap memiliki manfaat yang berbeda. Laktat mendeteksi iskemia dan mencerminkan metabolisme jaringan, sedangkan glukosa memantau metabolisme energi dan status kesehatan sistemik. Kombinasi keduanya meningkatkan tingkat keberhasilan free flap. Dengan ketersediaan alat yang memadai, pendekatan ini berkontribusi pada peningkatan kualitas perawatan pasien dan hasil bedah rekonstruktif yang lebih baik.

Kata Kunci: *Pemantauan Free Flap; Laktat; Glukosa; Metabolisme Jaringan; Kecerdasan Buatan.*

Conflicts of Interest Statement:
The author(s) listed in this manuscript declare the absence of any conflict of interest on the subject matter or materials discussed.

INTRODUCTION

Reconstructive microsurgery techniques with free flap is widely used for restoring severe soft tissue and bone defects. It aims to maximize functional and aesthetic outcomes, minimize donor morbidity, and prevent infections while having sufficient soft tissue coverage for critical organs. Free flap offer a variety of tissue types, such as skin, muscle, bone, nerves, or a combination thereof and allow the reconstruction of sizeable tissue defects. The indications for free flap surgery, therefore, are broadly defined, ranging from congenital anomalies through burn injuries and cancerous lesions to severe trauma-related tissue defects. There is a wide range of workhorse flap options to suit the needs of the defect. For example, the radial forearm flap, the latissimus dorsi flap, the anterolateral thigh flap, the fibula free flap, and the rectus abdominis flap.[1-3]

One of the main concern of free flap procedure is flap ischemic time. It is well known that after a certain period of ischemia, irreversible changes occur to the flap that can lead to necrosis and failure. Some of possible risk factors, including age, sex, defect location, and comorbidities (diabetes, cardiovascular disease, hypertension, renal disease, smoking, alcohol use, and history of radiotherapy and chemotherapy), and additional potential risk factors, such as peripheral vascular disease, hyperlipidaemia, American Society of Anaesthesiologist's classification, operative time, and anticoagulant medications such as aspirin, clopidogrel, and low-molecular-weight heparin.[4,5]

Several study before showed the survival rate of free flap salvage procedure is up to 70%-80%. In 11 studies Shen et al had reviewed, one of the factors that can decrease the salvage rate is the increasing of the time between free flap and salvage procedure.[7-9] The failure of free flap procedures can present in various ways. Common signs of flap failure include compromised blood flow, which can manifest as colour changes in the flap (e.g., pallor, cyanosis), temperature differences (cooler or heat), and capillary refill time (increase or delay).[6] Tissue necrosis or death can occur if the blood flow of artery and vein in flap does not balance, non-viable tissue. Increase of decrease of free flap turgor, swelling, increased pain, and discharge, can also signal flap failure. Additionally, hematoma or seroma formation, where blood or fluid accumulates under the flap, can compromise its viability. Dehiscence, the separation of the wound edges or the breakdown of the flap, and partial or complete flap loss requiring further surgical intervention, are severe indications of flap failure.[10]

Several factors influence the failure of flap procedures in reconstructive surgery, including patient-related factors such as age, comorbidities (e.g., diabetes, cardiovascular diseases), smoking, and nutritional status, which can affect wound healing and blood flow. Surgical factors, such as the choice of free flap, surgical technique, and intraoperative handling, play a critical role.[11] Postoperative care, including flap monitoring for early detection of compromised blood flow and timely intervention, is also crucial. Additionally, external factors like infection, hematoma, or seroma formation can lead to increased tension and compromised blood supply, contributing to flap failure. Proper patient selection, meticulous surgical technique, and diligent postoperative care are essential to minimize the risk of flap failure.[12]

Measuring changes in oxygenation and perfusion of the flap is essential. Decreased tissue oxygen levels increase glycolysis and lactic acid accumulation which is associated with a decrease in pH and subsequent activation of the

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complement system. The critical ischemia time is the maximum length of time that can tolerate ischemia and allows the tissue to remain viable after reperfusion. Apart from ischemia itself, another causative factor that can lead to tissue loss is called ischemia or reperfusion injury, an inflammatory reaction that occurs after an episode of ischemia when blood flow is restored.[13]

Under aerobic conditions, pyruvate is produced through glycolysis and then enters the Krebs cycle, mostly through the production of lactate. In case of ischemia, the glucose molecule is metabolized to pyruvate or as known as anaerobic glycolysis and is activated due to lactate accumulation. Lactate enters the Cori cycle as a substrate for gluconeogenesis. Vascularization of a flap experiencing hypoxia can cause a shift in metabolism from aerobic to anaerobic, resulting in pyruvate being formed which is then converted into lactic acid. [14, 15]

Microdialysis is a method that measures certain metabolites like glucose, lactate, etc., levels in the flap blood. Peripheral lactate concentrations can be detected in small volumes of blood via portable devices commonly used in the ICU. Monitoring of capillary glucose levels in free flaps using glucometer is being proposed as a cheap, rapid, and simple method for the early prediction of microvascular complications and thereby reducing flap failure. Peripheral lactate concentrations and glucose level can reflect the condition of an ischemic flap and detect tissue hypoperfusion as a predictor of tissue death.[16,17]

Plastic surgery is one of the main focus areas of the artificial intelligence technology revolution. Artificial intelligence has a much wider range of applications and potential advantages as it can influence every stage of the patient journey, from initial evaluation to post-operative monitoring.

In accordance with the advancement of technology, flap viability assessment using simple tools will be more practical with the help of artificial intelligence. In addition, the assessment is done objectively, without the bias of the observer's experience. The purpose of this study is to obtain an overview of previous studies and to obtain a theoretical basis for using artificial intelligence, peripheral lactate and glucose examination as free flap viability assessment.

METHOD

The primary database utilized to retrieve the salient medical literature presented in this study were using book reference and Google Scholar, Pubmed, also Science Direct. The search terms used both separately and in combination included “free flap” or “microsurgery flap” or “free tissue transfer” or “tissue transplantation” and “viability” or “ischemia” or “ischemic” or “thrombus” or “thrombosis” or “hypoperfusion” and “lactate” or serum lactate” or “peripheral lactate” or “lactic acid” or “anaerobic metabolism” or “acidosis” or “artificial intelligence in plastic surgery”. Only articles in English and published less than ten years were included.

RESULTS AND DISCUSSION

Lactate is produced during anaerobic metabolism, which occurs when tissues do not receive enough oxygen. Under normal aerobic conditions, cells produce energy (ATP) primarily through oxidative phosphorylation. However, when oxygen supply is insufficient, cells switch to anaerobic metabolism, resulting in the production of lactate. [18]

Elevated lactate levels in tissue or blood can indicate that the tissue is not receiving enough oxygen and is undergoing anaerobic metabolism. This makes lactate a useful marker for detecting hypoxia in tissues, including surgical flaps. Lactate levels can be measured using blood samples taken from the tissue flap or from the peripheral circulation. Point-of-care testing devices allow for quick and easy measurement of lactate levels at the bedside, providing immediate feedback to the surgical team.[19]

During flap surgery, real-time monitoring of lactate levels can help surgeons assess the adequacy of blood flow and oxygenation to the flap. Adjustments can be made on the spot to improve perfusion if needed. After the flap has been attached, regular monitoring of lactate levels can detect early signs of compromised blood flow or oxygenation. This allows for prompt interventions to address issues before they lead to flap failure. Studies have shown that high lactate levels correlate with an increased risk of flap failure. Monitoring lactate provides a predictive tool that can help guide clinical decisions, such as whether to perform additional surgical interventions or modify postoperative care.[19,20]

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In the cytoplasm, glycolysis generates the intermediate metabolite pyruvate. In aerobic conditions, pyruvate transforms into acetyl CoA to enter the Kreb's cycle, while in anaerobic conditions, pyruvate is converted to lactic acid by lactate dehydrogenase (LDH). In aqueous environments, lactic acid mostly dissociates into lactate and H ions, with lactate being the prevalent form. The terms lactic acid and lactate are often used interchangeably. Lactate in plasma is buffered by NaHCO.

Lactate is produced by various tissues including erythrocytes, perivenous hepatocytes, skeletal myocytes, and skin, with a basal production rate of 0.8 mmol $kg^{-1}h^{-1}$ (equivalent to 1300 mmol day-1).[21]

The study in French found that combined lactate and glucose thresholds demonstrated high sensitivity and specificity in detecting pedicle impairment. However, false positive and negative measurements highlighted monitoring complexities. Elevated lactate and glucose levels preceded clinical diagnoses of vascular complications, indicating their potential as early warning indicators.[22]

Another French study observed fluctuations in capillary lactate and glucose levels during simulated thrombosis, suggesting their potential as supplementary tools for postoperative clinical monitoring of free flaps. Average lactate and glucose levels in flap capillaries closely mirrored those in systemic blood, validating the pig model's relevance despite minor variances potentially attributable to animal stress. [20]

Monitoring capillary glucose and lactate levels could trigger early suspicion of vascular thrombosis, with disparities between healthy and ischemic flaps observable from the outset. Combining these measurements could accelerate complication detection and bolster flap survival rates post salvage surgery, improving diagnostic precision and efficacy. Additionally, the straight forwardness of current techniques for assessing these parameters makes them practicable for healthcare professionals. Nonetheless, threshold levels were not determined in this study to mitigate the risk of statistical bias, necessitating further exploration in future investigations.[23,24]

Glucose measurement in free flap monitoring provides several advantages over lactate measurement. Firstly, as a primary energy source for cells, glucose levels reflect metabolic activity and energy status within the flap, offering insights crucial for tissue viability and function. Additionally, glucose is readily available in the bloodstream, allowing for quick measurement and timely interventions in response to metabolic fluctuations. Abnormalities in glucose levels can indicate underlying metabolic dysregulation or physiological stress, aiding in the early detection of complications and providing valuable diagnostic information. Moreover, glucose monitoring is a routine practice in clinical settings, making it familiar to healthcare providers and easily integrated into existing monitoring protocols. Finally, glucose levels can reflect systemic health status and comorbidities, guiding perioperative management strategies to optimize surgical outcomes and patient care. Overall, glucose measurement offers unique insights into tissue metabolism, energy status, and systemic health, complementing lactate measurement in free flap monitoring and enhancing clinical decision-making.

Lactate measurement in free flap monitoring surpasses glucose measurement in several aspects. Firstly, it serves as an early indicator of ischemia, rising promptly during tissue hypoxia or compromised blood flow, enabling timely intervention to salvage the flap. Secondly, lactate directly reflects tissue metabolism, offering real-time insights into tissue perfusion and viability. Unlike glucose, lactate is less reliant on vascular supply, providing a more reliable assessment of tissue metabolism under compromised conditions. Additionally, elevated lactate levels quantitatively correlate with the severity of ischemic insult, facilitating risk stratification and tailored interventions. Moreover, lactate measurement can be minimally invasive, allowing for frequent monitoring without significant patient discomfort. Overall, lactate measurement offers a sensitive and specific approach to free flap monitoring, enhancing the detection and management of complications and ultimately improving surgical outcomes.

However, the traditional reliance on laboratory testing for these biomarkers can lead to delays in obtaining results, which may compromise the precision of postoperative monitoring. In many cases, results may take hours to become available, hindering timely clinical decisions and interventions.[25]

Artificial intelligence is a powerful paradigm that is rapidly impacting every aspect of our daily lives and scientific research. It is undergoing interdisciplinary transformations including tissue engineering. Artificial intelligence offers several advantages, such as

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lower costs and faster results, compared to other medical research approaches, namely clinical and laboratory methods. For example, predictive modelling involves the use of data to predict future outcomes based on unforeseen data, with the aim of advancing personalised medicine and optimising treatment strategies. Predictive modelling plays a critical role by providing insights in areas as diverse as predicting disease progression, identifying patients at risk of developing certain conditions, and optimising treatment plans.[26]

One of focus areas of artificial intelligence technology in medicine can be affected in Plastic Surgery, that has a much wider range of applications and potential advantages as it can influence every stage of the patient journey, from initial evaluation to post-operative monitoring. For example, the potential to predict free flap viability by measuring post-operative lactate with artificial intelligence tools. This optimizes clinical efficiency and allows plastic surgeons to perform more precise post-operative monitoring.[27,28]

Ideal flap monitoring tools should be objective, reliable, sensitive, and simple. Further research, regulations, and efforts to enforce ethical standards are necessary because artificial intelligence inevitably has limitations and must be tested until it is well established. Data protection and privacy is therefore a major issue, because any integration of artificial intelligence is likely to involve the transfer of confidential patient information to third parties that develop and manage the software.[29,30]

CONCLUSION

In conclusion, peripheral lactate monitoring plays a crucial role in assessing the viability of tissue flaps in reconstructive surgery. By providing early indications of tissue hypoxia and potential ischemia, lactate levels help clinicians make timely decisions to ensure flap survival. This improves overall surgical outcomes and reduces the risk of complications, making lactate an invaluable tool in the management of tissue flaps. The simplicity and accessibility of existing techniques to measure these parameters are feasible for routine clinical use but remain potential for development utilising artificial intelligence.

Overall, a comprehensive approach that combines lactate and glucose measurements offers valuable insights into tissue metabolism, energy status, and flap viability, ultimately enhancing patient care and surgical outcomes in reconstructive surgery.

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