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SHORT REPORT

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Transcutaneous near-infrared spectroscopy (NIRS) for monitoring kidney and liver allograft perfusion

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Abstract

Background: The use of transcutaneous near-infrared spectroscopy (NIRS) for monitoring the perfusion of kidney and liver allografts has been proposed in the last years. This device might detect an early decrease in allograft oxygenation allowing prompt detection of vascular complications.

Methods: A systematic review of the literature about the use of transcutaneous NIRS in monitoring allograft perfusion was performed according to the PRISMA guidelines.

Results: The authors screened 1313 papers. The search yielded five pertinent articles. Three of them reported the experience of NIRS in kidney transplantation and the other two dealt with its use in liver transplantation, for a total of 55 paediatric patients and 121 adults. In the studies concerning kidney transplantation, NIRS measurements were significantly related to serum creatinine, estimated glomerular filtration rate (eGFR), urinary neutrophil gelatinase-associated lipocalin (u-NGAL), serum lactate, resistive index assessed by Doppler-ultrasonography and systolic blood pressure. The two studies dealing with liver transplantation found a significant decrease in liver regional oxygenation, assessed by NIRS, before the occurrence of vascular complications.

Conclusions: Preliminary studies have related NIRS monitoring to kidney and liver allograft perfusion, both in adults and children. Further investigation is needed to establish the normal range of NIRS values and the factors influencing NIRS monitoring.

1 | INTRODUCTION

Kidney transplantation (KT) has become the treatment of choice for paediatric end-stage kidney disease.[1] Nevertheless, in comparison to adults, the small calibre of the vessels and the common size-mismatch between donors and recipients can predispose to vascular complications including allograft thrombosis. The latter may affect up to 10% of KTs and account for 35% of allograft losses in the first year.[2] Similar considerations might be made when dealing with liver transplantation (LT). Even in this case, early vascular complications may affect up to 25% of the grafts.[3] Therefore, prompt recognition and treatment are clearly essential for the preservation of the allograft.

Vascular complications have no specific clinical or biochemical signs allowing for early diagnosis. Doppler-ultrasonography (DUS) and scintigraphy, for KT, are reliable tools to assess allograft perfusion,[4] but do not allow continuous monitoring of the allograft and can miss early diagnosis, even if performed with a strict schedule in early follow-up.[5]

Transcutaneous near-infrared spectroscopy (NIRS) allows for non-invasive, real-time, continuous monitoring of regional oxygenation of the hemoglobin (rSrO2), which is an indirect measure of the blood flow and the metabolic state, of tissue placed deeper beyond the skin. Several clinical studies have tested the use of NIRS for monitoring cerebral and somatic perfusion in intensive care units [6] and

TABLE 1 Clinical studies assessing the feasibility of real-time NIRS monitoring of allograft perfusion

Study	Country	Design	Population	NIRS monitoring	Values of allograft rSrO2	Adverse events	Main findings
Vidal et al[8]	Italy	Prospective	24 paediatric kidney transplants	72 h after transplant	At the beginning: 68.8% (IQR 59.3-76.2) At the end: 83.6% (IQR 79.2-90.4)	4 delayed graft functions	rSrO2 correlated with serum creatinine, eGFR and u-NGAL.
Malakasioti et al[11]	UK	Prospective	29 paediatric kidney transplants	2 min (during annual or biannual routine follow-up)	Upper pole: 78.8% ± 7.0% Lower pole: 79.3% ± 10.7%	None reported	rSrO2 correlated with resistive index by DUS and systolic blood pressure.
Shiba et al[16]	Japan	Case Report	2 paediatric liver transplants	After the transplant until the discharge from Intensive Care Unit	Case 1: decline of 23% Case 2: decline of 26%	2 acute cellular rejections	Decrease in rSrO2 anticipated vascular complications.
Pérez Civantos et al[14]	Spain	Prospective	61 adult kidney transplants	24 h after transplant	At the beginning: 81% ± 6% At the end: not statistically different	3 bleedings 1 arterial thrombosis 1 venous thrombosis	Decrease in rSrO2 anticipated vascular complications. rSrO2 correlated with serum lactate and initial diuresis.
Pérez Civantos et al[15]	Spain	Prospective	50 adult liver transplants	24 h after transplant	At the beginning: 74% ± 5.7% At the end: 76% ± 4.1%	12 bleedings 2 low cardiac outputs 1 septic shock 1 bronchospasm	Decrease in rSrO2 anticipated vascular complications.

the viability of soft-tissue flaps.[7] Recently, it has been proposed for the surveillance of allograft perfusion too.[8]

A systematic search of the literature was performed, aiming to identify the current evidence on the in vivo application of NIRS for the monitoring of allograft perfusion. The findings might be useful for future research to implement the large-scale use of NIRS.

2 | MATERIALS AND METHODS

The systematic review was performed according to the PRISMA guidelines.[9] PubMed, Scopus and The Cochrane Library were searched in November 2020, using a combination of terms including "near-infrared spectroscopy," "NIRS" and "transplantation." The search was limited to English language and publications from 1991 to 2020. Studies including animal models were excluded.

3 | RESULTS

Overall, 1313 papers were screened. The search yielded five pertinent articles (Appendix A). Three of them investigated kidney graft perfusion, accounting for a total of 53 paediatric patients and 50 adult patients. The remaining two papers dealt with 50 adults and two children undergone LT. The quality assessment, according to the Newcastle-Ottawa Scale, showed a high risk of bias for all studies (Appendix B). This might be because of the small size of the cohorts selected for the studies. Main findings of the selected papers are summarised in the Table 1. NIRS monitoring was used maximum for the first 72 hours after transplant in a cohort of children undergone KT. The reference values of rSrO2 were reported in four of the studies and these were quite variable. Adverse events were generally rare, but most of the studies find a correlation between abnormal NIRS values and complications with a decrease in organ perfusion for both KT and LT.

4 | DISCUSSION

A preliminary study by Vidal et al reported transcutaneous NIRS measurements in 24 children after KT.[8] Kidney rSrO2 measured by NIRS significantly increased over time during the first 3 days after surgery and a significant correlation was found with serum creatinine, estimated glomerular filtration rate (eGFR) and with the decrease of post-operative urine-neutrophil gelatinase-associated lipocaine (u-NGAL), which is a marker of tubular injury reflecting the ischemic and reperfusion damage of the kidney. In this series, DUS did not identify any abnormality in kidney vascularisation and no vascular complications were reported. To date, four patients experienced a delayed graft function (DGF) without any peculiar modifications of rSO2.

Despite these promising results, Skowno et al raised some criticisms.[10] First, DUS, the gold standard for the assessment of allograft perfusion, was not related to rSrO2. Recently, Malakasioti et al identified a significant correlation between kidney rSO2 measured by NIRS and resistive index derived from DUS in a series of 29 paediatric patients.[11] Once again, no complications were reported in this cohort.

Second, the region of interest of NIRS may reach up to 4 cm below the skin, according to the manufacturers, and its effectiveness in monitoring somatic perfusion was validated in infants weighing less than 10 kg.[12] This body weight was sensibly lower than those of the patients undergone KT or LT. However, Skowno et al confirmed the effect of body size on transcutaneous NIRS only in a porcine model, suggesting its in vivo application up to 1 cm of depth.[13]

Nevertheless, Pérez Civantos et al assessed renal rSrO2 in 61 adults who undergone KT, using probes with a maximum depth of 2.5 cm.[14] NIRS readings were significantly correlated with the decreasing values of serum lactate for 8 hours and 24 hours, which is another marker of ischemic injury. Furthermore, kidney rSrO2 was related to initial diuresis for 3 hours and to mixed central venous oxygen saturation. Moreover, no correlation with DUS was found. In addition, in this series, arterial thrombosis and bleedings were encountered, showing a maintained decrease in rSrO2 which might anticipate the vascular events.

It is relevant to point out that the same study was replicated in liver transplantations. Even in this scenario, NIRS decreased early during bleeding or in case of thrombosis.[15]

The last concern about NIRS regarded the placement of the probes. The vascularisation over the surgical wounds may be altered by the healing process. Skowno et al speculated that a placement directly over that area might influence NIRS readings.[10] Therefore, experimental studies on reliable animal models, such as rats or piglets, should better clarify the real impact of abdominal wall thickness and of the healing process on transcutaneous NIRS monitoring.

Moreover, the normal range of rSrO2 values needs to be established by investigating a larger number of patients. Only after this process, NIRS might help in the prompt identification of acute adverse events, which is the final aim of real-time NIRS monitoring. At the moment, NIRS contributed to the early diagnosis of vascular complications in two children who undergone liver transplantation.[16] However, even if kidney rSrO2 was not altered amongst the patients affected by DGF in the series by Vidal et al, the authors suggested that NIRS might help in discriminating the causes of oligo-anuria in the early post-operative time after KT, helping in managing the post-operative fluid balance.[8]

Recently, an experimental study successfully tested a NIRS wireless device implanted on the surface of the kidney. The study was conducted on pig models after surgical intervention of autotransplantation. During 48-hour monitoring, the device detected the decrease of kidney perfusion with a 100% sensitivity, proving the efficacy of the NIRS technique in identifying potential complications. However, the main concern about this tool involves the need for a second intervention for its removal. This might be considered too invasive, especially in the paediatric population, and might not

be free from complications, even if no adverse events were reported during this procedure.[17]

Further investigation should also relate rSrO2 to perfusion renal scintigraphy. Even if this is a point-evaluation of allograft perfusion, this is the most objective modality to assess both kidney vascularisation and function, also adding information about the early prognosis of the KT.[18]

Before large-scale in vivo utilisation, experimentation of NIRS on animal models might investigate factors influencing the measurements of both kidney and liver rSrO2, such as the depth of the region of interest and the correct transcutaneous placement of the probes. Furthermore, selected cohorts of patients might help in defining the normal values of both kidney and liver rSrO2.

In conclusion, preliminary studies showed the correlation between NIRS, graft function and graft perfusion in both adult and paediatric KTs. As to LT, no prospective studies were found in paediatric population, but an adult cohort showed encouraging results.

DISCLOSURE

None declared.

AUTHORS' CONTRIBUTIONS

All Authors contributed to the study conception and design. FG and MC performed the literature search and the screening of the papers. FG and MC wrote the first draft of the manuscript. EB, PZ, AA and PG critically reviewed and commented on the previous version of the manuscript. All authors read and approved the final manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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