Transplant International

REVIEW

Evaluation of donor kidneys prior to transplantation: an update of current and emerging methods

Beat Moeckli[1], Pamela Sun[2], François Lazeyras[3], Philippe Morel[2], Solange Moll[4], Manuel Pascual[5,*] & Léo H. Bühler[2,*]

1 Department of Surgery and Transplantation, Zurich University Hospital, Zurich, Switzerland
2 Department of Surgery, Geneva University Hospital, Geneva, Switzerland
3 Department of Radiology and Medical Informatics, CIBM, Geneva University Hospital, Geneva, Switzerland
4 Department of Pathology, Geneva University Hospital, Geneva, Switzerland
5 Transplantation Center Lausanne, University Hospital and University of Lausanne, Lausanne, Switzerland

Correspondence
Beat Moeckli MD, Universitätsspital Zürich, Rämistrasse 100, 8091 Zürich, Switzerland.
Tel.: 0041 79 649 47 10;
fax: +41 44 255 44 49;
e-mail: beat.moeckli@gmail.com

*Authors with equal contribution.

SUMMARY

The lack of suitable kidney donor organs has led to rising numbers of patients with end stage renal disease waiting for kidney transplantation. Despite decades of clinical experience and research, no evaluation process that can reliably predict the outcome of an organ has yet been established. This review is an overview of current methods and emerging techniques in the field of donor kidney evaluation prior to transplantation. Established techniques like histological evaluation, clinical scores, and machine perfusion systems offer relatively reliable predictions of delayed graft function but are unable to consistently predict graft survival. Emerging techniques including molecular biomarkers, new imaging technologies, and normothermic machine perfusion offer innovative approaches toward a more global evaluation of an organ with better outcome prediction and possibly even identification of targets for therapeutic interventions prior to transplantation. These techniques should be studied in randomized controlled trials to determine whether they can be safely used in routine clinical practice to ultimately reduce the discard rate and improve graft outcomes.

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Introduction

End stage renal disease (ESRD) represents a major public health concern for our society. Renal transplantation increases patient survival, improves quality of life, and is cost-effective even for high-risk donor organs [1–3]. Unfortunately, a mismatch between available donor organs and patients on ESRD waiting lists restricts the access to kidney transplantation, with now close to 100 000 patients awaiting organs in the United States alone [4]. Despite the shortage, the rate of discarded kidneys is as high as 17–20% [4], with recent data suggesting that some of these discarded organs could be used safely with comparable outcomes to transplanted organs [5–7].

With an ever-increasing number of patients on the waitlist and a stagnant number of organs available for transplantation, there is a pressing need to increase the longevity of transplanted grafts and decrease the number of unnecessarily discarded kidneys. This requires an interdisciplinary, multifaceted approach with a thorough assessment of higher risk kidneys before allocation, as

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recently outlined by Wekerle *et al.* [8]. Although a broad array of assessment methods and markers exists, none have been shown to consistently predict post-transplantation outcomes nor have been widely accepted in clinical practice. With the absence of international consensus guidelines, transplant teams have few objective measures and are often left with their clinical experience to accept or reject organs. This is highlighted by a wide variance in the rate of discarded organs amongst different institutions even within the same country [9]. The purpose of this review is to give an overview of advantages and limitations of the currently available tools and an outlook on emerging methods of objective appraisal of organ quality.

Current methods

Clinical scores

Naturally, clinical parameters of the donor can be utilized to predict graft function as they are often readily available and do not require invasive nor time-consuming testing of the kidney. Thus, several scores have been developed based on US registry data such as the Expanded Criteria Donor classification [10] or the more elaborate Deceased Donor Score [11] or Donor Risk Score [12]. The limitations of these classification systems are the dichotomous nature of the Expanded Criteria Donor classification, their limited clinical applicability and inadequate predictive power. A single center observational study comparing the predictive power of these different scores only found the Donor Risk Score to be significantly associated with serum creatinine at 1 year after transplantation. The predictive power was moderate at best with an area under the curve of a receiver operator curve (AUC) of 0.67 [13].

In an attempt to create a more comprehensive score to predict graft outcomes, Rao *et al.* developed the kidney donor risk index (KDRI). They analyzed a national database of almost 70 000 first-time deceased donor transplants and proposed a score including ten donor-specific characteristics available at the time of transplantation (including age, terminal creatinine, and hepatitis C virus serostatus) [14]. The KDRI for a specific organ is calculated in comparison to a reference donor with a higher score conferring a higher risk for graft failure. While the overall AUC for predicting graft survival is a modest 0.62, the KDRI allows a stratification of organs along percentiles. For clinical indication the KDRI is remapped into cumulative percentage scale, the Kidney Donor Profile Index (KDPI), where a donor with a KDPI of 80% has a higher expected risk for graft failure than 80% of the donor organs recovered during the previous year. The highest KDPI quintile has an expected graft survival at 10 years of 33.9% compared to 60.9% in the lowest quintile [15]. The strength of the KDRI/KDPI thus lies in predicting graft survival at the extremes of the spectrum of donor/organ characteristics. It has been validated both externally and temporally in the United Kingdom and the Netherlands [16,17] and is currently the most widely used clinical score with the Organ Procurement and Transplantation Network using it for allocation of kidneys in the US [18]. The main shortcoming of clinical scoring systems, however, remains their low predictive accuracy overall.

Histological evaluation

The pretransplantation histology is currently one of the most widely used and studied graft evaluation methods. This is especially true for the US where up to 85% of higher risk kidneys are assessed histologically in contrast to Europe where this rate is much lower [19]. In an attempt to improve reproducibility and objectivize the histological assessment, several composite histological classifications were developed including the Banff criteria [20], the Maryland Aggregate Pathology Index [21], the Chronic Allograft Damage Index, and the Remuzzi score [22]. With all histological evaluations however, there are still uncertainties in sampling, processing, and evaluating the biopsies.

Technical aspects

While most reports of prognostic value of preimplantation donor kidney biopsies are based on paraffin sections (PS), frozen sections (FS) are used in the majority of institutions. FS has the advantage of being less resource intensive and requires merely 30 min to prepare in comparison to over 3 h for PS, thereby minimizing prolonged cold ischemia time; however it is unclear how the quality compares to PS (Fig. 1). Sagasta *et al.* [23] compared the Remuzzi score initially obtained by the on-call pathologist, with the score retrospectively given for the same slide by a trained pathologist. In addition, they compared the originally obtained score on a FS with a retrospectively assessed score on a PS for the same tissue. They found higher agreement between different techniques than between observers, suggesting that the training of pathologists has a more significant impact on accuracy than processing methods. Other studies have also confirmed low

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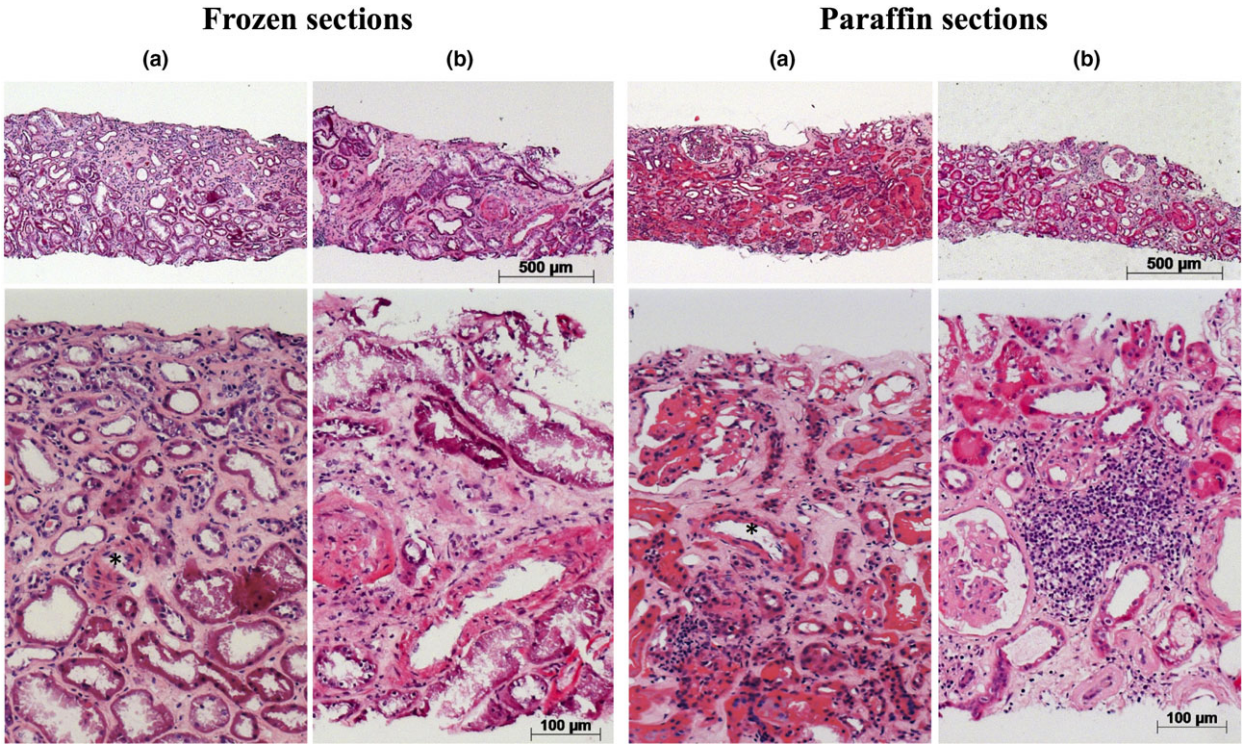

Figure 1 Renal biopsy with frozen and paraffin sections. Two renal biopsies (a and b) with frozen and paraffin sections. (a) High quality frozen section with a Remuzzi score identical to the formol section: Glomerular global sclerosis (0), tubular atrophy (2+), interstitial fibrosis (2+), arterial and arteriolar narrowing (0) * marks an arteriole. (b) Poor quality frozen section with a Remuzzi score identical the formol section: glomerular global sclerosis (2+), tubular atrophy (2+), interstitial fibrosis (2+), arterial and arteriolar narrowing (0). Magnification 25× and 100×.

reproducibility of the histological score between a trained renal pathologist and the on-call pathologist [24].

Other critical questions in the evaluation of organs by histological scores are whether the material provided by biopsies is representative of the entire kidney and whether needle biopsies (NB) or wedge biopsies (WB) is the better tissue sampling method. Mazzucco *et al.* [25] compared the Remuzzi scores obtained by NB and WB with the score obtained from tissue of the entire kidney of 154 organs that were not transplanted. They found that NB had a higher overall concordance with the state of the whole kidney (*k*-index of 0.73; 95% CI, 0.62–0.84) than WB (*k*-index of 0.57; 95% CI, 0.29–0.85) and is a closer approximation of the state of the whole organ. These results indicate that NB, with the advantage as the less invasive method, is probably the preferred method of kidney tissue sampling.

Association of histological scores and graft outcomes

The most important question is how well the histological findings correlate with and predict the long-term clinical outcomes of a transplanted organ. Many of the studies on this topic are of modest quality and are generally characterized by a high heterogenicity in endpoints studied, technical aspects and histological scores used [26]. While some studies showed a correlation between composite histological scores and graft survival [27,28], others did not [29–31]. In the largest study to date, a registry analysis by Sung *et al.* including 12 536 higher risk kidneys, no association between glomerulosclerosis and graft survival was shown, but a weak association between glomerulosclerosis and creatinine clearance at 1 year. As a registry analysis, the study suffered from selection bias. Two more recent studies compared the predictive performance of a clinical score with the performance of a histological score and found no improvement in prediction of post-transplant allograft survival beyond the moderate prediction provided by the clinical data [32,33]. In 2006, Remuzzi *et al.* [34] found that graft survival of donor organs that were attributed for single or dual transplantation based on biopsy findings did not differ significantly from those of grafts from donors under the age of 60 years, but were superior to those of grafts from older donors which were not evaluated histologically (hazard ratio for graft failure of older donor not evaluated histologically to those evaluated histologically, 3.68; 95% CI, 1.29–10.52;

$P = 0.02$). In a more recent study by the same group, the authors demonstrated good outcomes from grafts from very old donors (>80 years old) that were evaluated histologically for single or dual transplantation [35].

In conclusion, the current literature fails to demonstrate the clinical utility of pretransplantation histological assessment of grafts. Its predictive performance is poor and there is even some evidence that suggests that the implementation of routine pretransplantation biopsies increases the rate of discarding potentially viable organs [9,36]. However a histological score could potentially deliver an improved prediction profile in conjunction with other innovative methods like molecular phenotyping [37]. Finally, given the discordance between practice and evidence, randomized controlled trials are needed to provide more information on the possible benefits and harms of routine histological assessment of grafts [38].

Machine perfusion

Charles Lindbergh developed in collaboration with the French surgeon and Nobel Prize winner, Alexis Carrel, an apparatus for the perfusion of whole organs in 1935 [39], but it was not until the 1960s when clinically applicable devices emerged and the first machine-perfused kidney was transplanted in 1968 [40]. Technological advances have provided the necessary solutions for portable and user-friendly devices, which are now commercially available.

A higher overall graft survival and lower rate of delayed graft function (DGF) may already justify the use of machine perfusion (MP). However, the question remains: *How efficient is MP in assessing the quality of an organ?* One study evaluating the reasons for discarding 12 536 ECD kidneys found that 15% of perfused kidneys were discarded partly based on high renovascular resistance (RR) [9]. Substandard perfusion dynamics are frequently used today as a criterion to discard donor kidneys, although the existing evidence on the true prognostic value of RR on graft outcome is scarce. In a large randomized controlled trial comparing hypothermic machine perfusion (HMP) to static cold storage (SCS) [41], the method of preservation was not disclosed at the time of the offer and the clinicians had no knowledge of the perfusion values. The decision to accept a given organ had to be based solely on conventional donor data, giving rise to the unique opportunity to elucidate the association between prospectively collected RR values and kidney graft outcomes [42]. RR at the end of machine perfusion was an independent risk factor for the later development of DGF but the predictive capacity of RR was relatively poor with statistical values unsuitable to make RR a stand-alone parameter to assess the risk of DGF. Another surprising finding of the study was that the six primary nonfunction (PNF) cases in their cohort had RR values that did not differ significantly from functioning kidneys. Applying a commonly used RR threshold would not have prevented a single case of PNF when eight viable kidneys (2.5%) would have been erroneously discarded.

In a Dutch study of 440 DCD kidneys from a single center perfused before transplantation, the effects of RR on graft outcome, and patient survival were examined. Their results supported those of Jochmans *et al.*; they found a significant and independent association between perfusion dynamics and graft outcomes with again a relatively low predictive value. Their results differed, however, in two ways; firstly, the Dutch study in contrast to that of Jochmans *et al.* found an association between RR and PNF, which is a more valuable graft outcome than DGF because of its closer association with graft failure in DCD kidneys. This finding could easily be explained by the higher number of PNF organs in the Dutch cohort ($n = 84$, 19.5%). Secondly, they used the RR values at the start of the perfusion instead of end-perfusion values, which could be advantageous as early viability assessment allows for early clinical decision-making. More recently, Parikh *et al.* conducted a prospective observational cohort study to examine the association between pump parameters and graft outcomes. They found the 1-h perfusate flow to be independently associated with DGF, however with a meager AUC of 0.57 [43]. Later studies by different groups have confirmed these results [44,45].

The currently available data show that there is an association between perfusion parameters and graft outcomes. This association, however, is not strong enough to make them suitable as stand-alone criteria. The fact that those values are readily available, noninvasive, and require no additional work-up, make them ideal to be used in conjunction with other available parameters in a global score. Here, the most promising approach seems to move away from clear perfusion cutoff values for the discard of organs and toward mapping of perfusion quality on a continuous scale similar to the KDPI.

Emerging techniques

Molecular biomarkers

There are a large number of emerging technologies that examine the function of an organ on a molecular level.

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Ranging from proteomics, metabolomics to transcription studies, these innovative methods help us to better understand ischemic-reperfusion injury mechanisms and immunologic or inflammatory processes [46]. Even though most of these molecular approaches are still at an early stage with relatively small-scale experiments and no validation in clinical trials, the potential for practice-changing discoveries in this field is promising. This section will focus on methods that may enter clinical practice in a foreseeable future.

Transcription analysis

In oncology, transcription analysis via quantitative PCR or microarray technology has been proven and validated to be a useful tool in predicting outcomes and personalizing therapy [47]. Albeit more recently, this has also been applied to the field of transplantation. The goal is to capture subtle changes in the transcriptome representative of injury to the graft that are potentially predictive of graft and patient outcome and otherwise undetectable based on histological or clinical assessment. Several groups have worked on gene expression analysis in renal tissues before transplantation as a marker for subsequent graft function with remarkable findings. In 2008, Mueller *et al.* [48] demonstrated that organs from living donors could be distinguished from deceased donor kidneys based on transcription analysis, a differentiation not possible on a classic histological evaluation. Not surprisingly and in accordance with results from other groups, the authors found genes involved in the complement cascade, immunity, and acute phase response up-regulated in kidneys with DGF compared to grafts with immediate function [49,50]. Scian *et al.* [51] identified and validated a set of three genes (i.e. CCL5, CXCR4, and ITGB2) up-regulated in preimplantation biopsies of kidneys that had a low glomerular filtration rate at 1-month post-transplantation. This could represent a first step toward identifying a small set of genes consistently expressed differentially in kidneys of suboptimal quality. In addition, McGuiness *et al.* [52] demonstrated that a simple score consisting only of two clinical indicators and the expression levels of two microRNAs involved in cellular bio-aging and damage response managed to predict DGF in 83% of the organs and performed considerably better than a widely used clinical score. Major flaws of the study included the use of DGF as a marker for outcome and an only partially successful validation of the results in an independent cohort. However, it demonstrated that gene expression analysis and clinical scores are complementary and technically feasible with a turnaround time of only 4 h for the molecular analysis. In a large, multicenter, prospective study, O'Connell *et al.* looked at the predictive power of expression analysis after transplantation. A transcription profile including 13 genes from biopsies collected at 3 months after organ implantation could not only reliably predict development of fibrosis at 12 months, but more importantly, it was associated with allograft loss at 2 and 3 years after transplantation, validated in two independent cohorts, and outperforming both clinical and pathological scores [53]. The integration of transcription analysis into routine medical practice can be seen in the addition of molecular assessment of transcripts to the 2013 Banff classification [54] but significant barriers to its routine use such as the lack of a true diagnostic gold standard, the absence of randomized controlled trials, and disagreement on which transcripts to measure remain.

Proteomic studies

Proteomics – the study of the entire set of proteins produced and modified by an organism – allows for drawing meaningful conclusions on the state of a specific organ. In transplantation, several proteins have been assessed. Neutrophil gelatinase-associated lipocalin (NGAL) is an acute phase protein that is briskly up-regulated in response to kidney injury and readily measured in serum and urine therefore lending itself as a biomarker [55]. Hollmen *et al.* [56] found elevated urinary NGAL to be an independent risk factor for prolonged DGF and associated with worse 1-year graft survival. However, NGAL failed to predict graft function and was directly correlated with creatinine levels. In a larger cohort of 1304 deceased donor organs, Reese *et al.* [57] examined the association between four different biomarkers and post-transplant graft function. The authors found all the examined proteins to be strongly associated with donor acute kidney injury but of limited predictive power for post-transplantation graft function. By combining NGAL, L-type fatty acid binding protein levels with serum creatinine, Koo *et al.* [58] successfully created a predictive score for DGF with an AUC of 0.808. This demonstrates once again that a single marker is highly unlikely to accurately reflect the complex processes determining the performance of a graft after transplantation.

Metabolomics

Metabolomics represents the quantitative analysis of low molecular weight compounds arising from metabolic

pathways present in a biological sample. Its potential has been demonstrated in a recent publication by Kostidis *et al.* In a post-transplantation setting, the authors identified the ratios of branched-chain amino acids over pyroglutamate and lactate over furamate as strong predictors for prolonged DGF (AUC of 0.85) 10 days after transplantation [59]. Two studies by different groups showed congruent results although with smaller patient numbers [60,61]. In a pretransplantation setting, Guy *et al.* looked at the differences in metabolic profiles in the perfusate of deceased donor kidneys to be transplanted. They found significant differences in levels of metabolites (gluconate, glucose, inosine, and leucine) between kidneys with or without later DGF as early as 45 min after the start of the perfusion [62]. A preclinical study in a porcine model showed similar results suggesting feasibility and clinical applicability [63]. The metabolomics approach to assess the quality of perfused organs bears several advantages; it can be performed safely, is easy and allows an objective, noninvasive assessment of an organ on a functional level. However, the current level of evidence is scarce and further large-scale trials are needed.

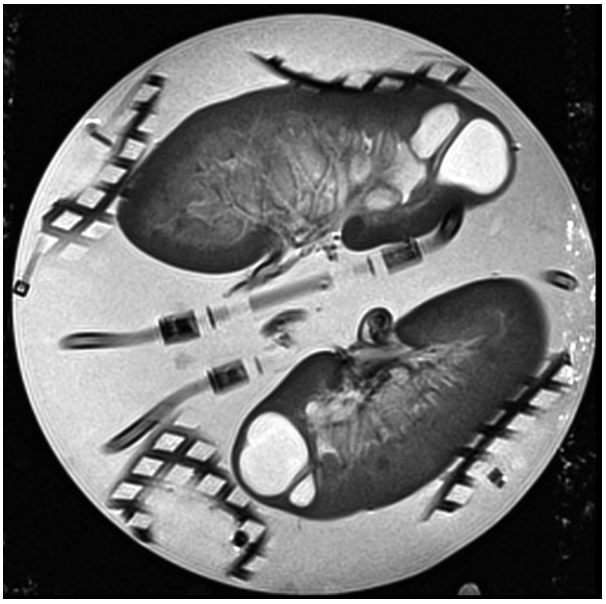

Figure 2 T2-weighted of 5 months porcine kidneys illustrating the presence of cystic tumors in both kidneys. Images were obtained at 3T (Siemens Prisma, Erlangen, Germany) inside the perfusion machine developed in Geneva [64]. Magnetic resonance imaging fast-spin-echo sequence was obtained with the following parameters: TR 5000 ms, TE 112 ms, 12 contiguous slices, slice thickness 3 mm, acquisition time 3 min 5 s.

Imaging

In 2007, Buchs *et al.* [64] developed at the University of Geneva a disposable perfusion machine that allows for oxygenated, hypothermic, pulsatile perfusion. It is unique in that it does not contain any ferro-magnetic materials in the perfusion module and therefore is compatible with magnetic resonance imaging (MRI) or spectroscopy. Our group has already published several preclinical studies focusing on two different aspects of magnetic resonance evaluation with promising results [65–68].

First, this technique allows for the acquisition of T2-weighted images and provides for the detection of major pathologies like tumors, abscesses or cysts that are not necessarily detected macroscopically (Fig. 2). Second, the perfusion of gadolinium enables the visualization of intra-renal microcirculation to discriminate between cortical and medullar circulation [68]. A cortico-medullary shunt is a sign of medullary ischemia [69,70]. This is remarkable because medullar ischemia is not otherwise detected by renovascular resistance measurements, yet it is potentially an important factor in graft function post-transplantation (Fig. 3). Gadolinium toxicity remains a concern, however ferumoxytol, an ultra-small iron oxide particle, has been successfully used as a nontoxic contrast agent for vascular evaluation in the renal transplant population and might represent an alternative [71,72].

The second aspect is organ viability assessment by magnetic resonance spectroscopy. Nearly three decades ago, Bretan *et al.* [73] showed that levels of ATP could be measured by ^{31}P magnetic resonance spectroscopy in kidney grafts. These authors proposed a ratio of ATP-precursors to inorganic phosphate as a representation of energy stores and as an indirect predictor of regeneration potential and therefore organ viability. In studies published by Buchs *et al.* [66] and Lazeyras *et al.* [67], the applicability of a new method to directly measure the production of ATP was demonstrated in porcine kidneys under oxygenated, hypothermic, pulsatile perfusion. The tissue's capability of ATP synthesis could be a promising biomarker for organ viability. In another preliminary study, Buchs *et al.* [68] showed that there is a correlation between the level of ATP re-synthesis in grafts and warm ischemia time. Nevertheless, the accuracy of these new methods to reliably predict transplantation function or outcomes still needs to be proven in clinical studies. We plan to assess the correlation of gadolinium perfusion sequences and ATP detection by magnetic resonance spectroscopy with clinical data and histopathological evaluation in kidneys of very old deceased donors (>70 years old).

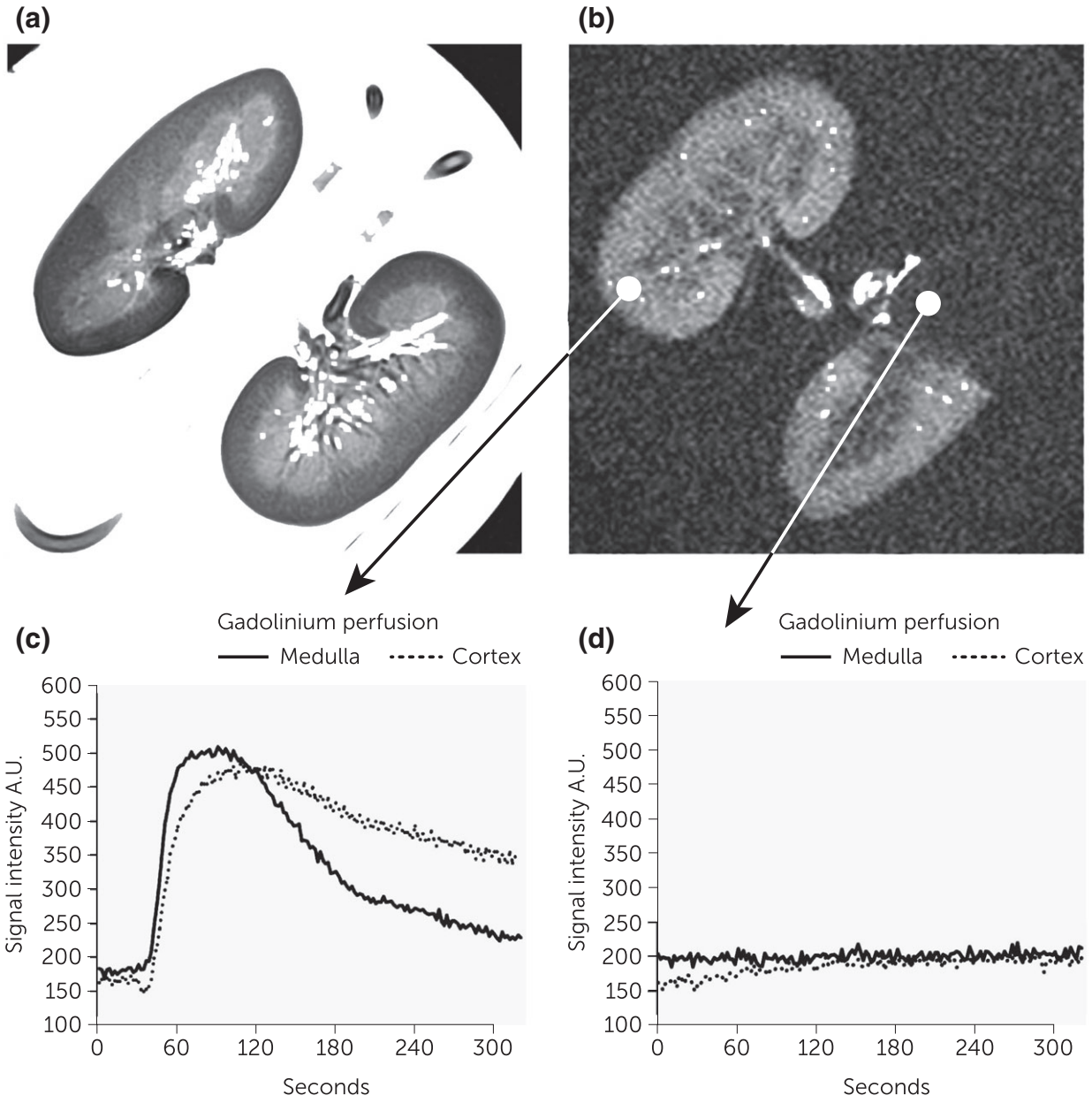

Figure 3 Magnetic resonance imaging perfusion imaging using gadolinium. The time course is illustrating well-perfused kidney (c) as well as kidney with absence of perfusion in one pole (d). Perfusion curves (c, d) are obtained from the region of interest located in the cortex and the medulla and reflect the dynamics of gadolinium inflow and outflow. It is of note that under normal conditions (c), cortical flow is more pronounced than medullar flow. Time onsets and descending slope provides valuable perfusion indices [68]. A T2-weighted anatomical image (a) and a T1-weighted image (b) illustrate the lack of perfusion in one kidney pole. The dynamic sequence used for the gadolinium perfusion study is a fast gradient echo with a preparation pulse, using the following parameters: TR 2000 ms, TE 1.3 ms, TI 240 ms, five slices (TR 400 ms per slice), slice thickness 4 mm, slice gap 1 mm, flip angle 12°, 160 measurements, total acquisition time 5 min 20 s.

Another imaging modality in assessing graft viability includes ultrasound, with spectral and color Doppler ultrasound already being used in the evaluation of the perfusion status of allografts after transplantation. More recently, contrast-enhanced ultrasound with the injection of microbubbles offers high-resolution mapping of the microvasculature of the kidney. Recent studies have shown success in the detection of small perfusion deficits and their correlation to later graft function [74,75]. Although no studies in a pre-transplantation setting exist to our knowledge, the integration of this relatively simple assessment method in conjunction with novel perfusion systems might merit consideration.

Ex-vivo normothermic perfusion

Ex-vivo normothermic perfusion (EVNP) is the most recent development in the field of machine perfusion. The main advantages of EVNP lie in its possibility to simulate physiologic conditions with both diagnostic and therapeutic options, i.e. the potential of assessing its function in a setting approximating the transplanted state as well as an active repair of the graft. This field is already extensively covered by recent reviews [76,77], in this work we focus solely on the utility of EVNP in assessing the quality of a renal grafts before transplantation. In a porcine model, the Toronto group demonstrated that kidneys perfused with a neonatal cardiopulmonary bypass technique under normothermic conditions for 8 h fared significantly better compared to kidneys preserved under SCS. Creatinine at 10 days was significantly lower in the *ex-vivo* perfused group compared to the SCS group [78]. In a later study, the same group demonstrated in a porcine model that routinely available parameters such as intra-renal resistance, acid-base homeostasis, and lactate clearance correlated with post-transplantation renal graft function [79]. Regarding the clinical application of EVNP, pioneers in the field, Nicholson *et al.* [80], performed the first kidney transplantation after normothermic perfusion in 2011. They later proposed a grading score of organs ranging from 1 to 5 (5 being the highest score) based on EVNP characteristics such as renal blood flow, macroscopic assessment, and total urine output [81]. In a clinical series including ECD and DCD donors, they demonstrated that the EVNP score correlates to post-transplantation outcomes with rates of DGF in kidneys with a total score of three at 38% compared to only 6% in kidneys with a score of one ($P = 0.024$) [81]. More importantly, the same group evaluated organs that were declined through the national organ sharing scheme. Of 55 kidneys declined and offered to the study, 10 were evaluated by EVNP with five successfully transplanted. Although this represents a modest yield, the authors delivered the proof of concept that the discard rate can be safely reduced with an intelligent organ quality evaluation strategy.

The main appeal of using EVNP for quality assessment is that an organ's function is restored and can be directly assessed instead of using surrogate markers. However, most of the current data are from preclinical or early clinical studies without long-term follow-up. A large multicenter randomized controlled trial is currently underway comparing EVNP to SCS and assessing organs during the perfusion. First results are expected for 2020 and will provide more clarity about the usefulness of EVNP in assessing kidney quality [82], similar to what is currently under investigation using *ex vivo* lung perfusion in lung transplantation [83].

Conclusion

There is currently a lack of an objective method to assess the quality of a donor organ prior to transplantation and to reliably identify kidneys of nonstandard quality suitable for transplantation to minimize the discard rate. In order to more accurately assess the risk for graft failure, the mechanisms involved need to be better understood. These are complex and include immunologic and nonimmunologic processes leading to graft dysfunction and subsequent silent events with progression to fibrosis [8]. This complexity is unlikely to be fully captured by a simplistic approach. However, a lengthy, resource-intensive process does not correspond to the needs of a transplant center and would be impractical to implement on a large scale. The challenge for the years to come will be to find highly accurate prediction tools that are simple to use and can be validated in large-scale trials. There is no such instrument on the horizon that will alone accurately predict the outcome of a specific organ. The most promising approach going forward is the combination of different techniques.

A promising candidate for such an integrative approach is transcription analysis. The technology is mature and has been shown in different settings to be of great value to the clinician [47,53]. Certain gene sets could be targeted, thereby precisely complementing information obtained through more established techniques like histopathology, perfusion analysis or simply clinical parameters as demonstrated by McGuinness *et al.* [52]. Another exciting field that has great potential for the future is EVNP. It can provide objective perfusion parameters about a certain donor organ as well as open up therapeutic opportunities for repairing a damaged organ. Donor kidneys not otherwise suitable for transplantation should be identified and studied for repair including the delivery of drugs, gene therapy or stem-cell therapy [81]. These techniques are still in their infancy but early results are very encouraging and with great potential [84,85].

A transplant team regularly faces a level of uncertainty regarding the quality of a kidney about to be implanted. Therefore, the research community needs to continue to explore the possibilities of the available and emerging techniques to improve the prediction accuracy. This could be one aspect in a multifaceted approach to increase the number of higher risk donor kidneys utilized for transplantation, decrease the rate of discarded organs, and most importantly, help ESRD patients waiting for a donor kidney.

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Conflicts of interest

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