RENAL transplantation is considered as the standard therapy for end-stage chronic kidney disease because it allows a better quality of life with a lower cost than dialysis. Although living donation has been shown as a valuable and safe response to shortage of organs for transplantation, a large majority of kidney transplantation is obtained from organ donation after brain death (BD). Quality of donor care is a major determinant of graft success and increases the number of eligible donors. Despite considerable efforts to improve quality of care for transplanted patients, 20 to 30% of delayed graft function (DGF, defined as a need for renal replacement therapy [RRT] within 8 days after transplantation) are usually reported after renal transplantation from deceased donors. As early recovery of graft function determines long-term graft survival, DGF is a fundamental prognosis variable. Expanded criteria for donors (ECD), especially age greater than 60 yr, could be a major explanation for DGF.

What We Already Know about This Topic
- Delayed graft function in renal transplant recipients still remains at 25%

What This Article Tells Us That Is New
- Despite the ability to predict acute renal failure earlier than serum creatinine rises in critically ill patients, neutrophil gelatinase-associated lipocalin measurements in blood samples obtained from brain-dead donors before kidney graft harvesting failed to predict either delayed or normal graft function in kidney recipients

ABSTRACT

Background: Delayed graft function is a major determinant of long-term renal allograft survival. Despite considerable efforts to improve donor selection and matching, incidence of delayed graft function remains close to 25%. As neutrophil gelatinase-associated lipocalin (NGAL) has been shown to predict acute renal failure, the authors tested the hypothesis that NGAL measurement in brain-dead donors predicts delayed graft function in kidney recipients.

Methods: In a prospective, multicenter, observational study, serum NGAL was measured in donors at the time of transfer to operating room. The primary endpoint was the delayed graft function, defined as the need for renal replacement therapy during the first week posttransplantation.

Results: Among 159 included brain-dead donors, 146 were analyzable leading to 243 renal transplantations. Of these, 56 (23%) needed renal replacement therapy. Donors' NGAL values were similar in case of both delayed and normal graft function in recipients. The area under the receiver-operating curve for NGAL to predict the need for renal replacement therapy before day 8 was 0.50 (95% CI, 0.42 to 0.59). The area under curve for NGAL to predict failure to return to a normal graft function at day 8 was 0.51 (95% CI, 0.44 to 0.59). Using multivariate analysis, NGAL was not associated to the need for renal replacement therapy (odds ratio, 0.99; 95% CI, 0.98 to 1.00) or failure to return to a normal graft function at day 8 (odds ratio, 1.00; 95% CI, 0.99 to 1.00).

Conclusion: NGAL measurement in brain-dead donors at the time of recovery failed to predict delayed or normal graft function in kidney recipients. (Anesthesiology 2015; 122:96-105)
for the high rate of DGF. Nevertheless, if ECD influence graft success, some studies surprisingly report only a slight difference of graft prognosis obtained from standard criteria donors versus ECD. These observations reflect the influence of other detrimental factors such as cold ischemic time, Human Leukocyte Antigen match, female sex, Caucasian origin, and the global quality of donor management. It has been demonstrated that cold ischemic time and DGF are two major factors of long-term renal allograft survival. Because DGF rate remains high, obtaining new criteria to predict DGF could be of particular interest to detect occult renal failure in brain-dead donors to improve donor–recipient matching. Recently, it was hypothesized that new biomarkers could better predict acute kidney injury (AKI) than classical markers such as serum creatinine or blood urea nitrogen. The neutrophil gelatinase-associated lipocaline (NGAL) was identified as a 25 kDa polypeptide chain of 178 amino acids that belongs to the lipocalin family of proteins and is produced by polymorphonuclear neutrophil cells and predominantly by renal tubule epithelial cells. In intensive care unit (ICU), NGAL predicts AKI 48 h earlier than serum creatinine and/or Risk, Injury, Failure, Loss, End-stage kidney disease classification criteria. The NGAL measurement could be also useful for assessing graft function after renal transplantation. In contrast, NGAL has been poorly studied to assess occult renal dysfunction in BD donors. Only one previous study reported that both urinary NGAL (U-NGAL) and serum NGAL (S-NGAL) failed to predict DGF in 99 BD donors. However, this previous study has several limitations: it was a monocentric study, with a potential center effect; measurement of S-NGAL was performed before the occurrence of BD in a significant proportion of patients (36%); and all patients were given glucocorticoids, which does not reflect the practice of all centers. These limitations justify a new multicenter study to clarify the usefulness of NGAL as biomarker in BD patients for predicting DGF in kidney recipients. Therefore, in the current study, we test the hypothesis that S-NGAL measurement in BD organ donors predicts DGF in kidney recipients.

Materials and Methods

Considering that the current study was noninterventional and that such investigation did not need significant additional blood sample (volume <0.5 ml), the institutional review board approved this study (Institutional Review Board, Nimes University Hospital, France, file number 2011.01.01) and stated that informed consent of next-of-kin was not required as organ donors are not considered human subjects. However, the next-of-kin was systematically orally informed and could refuse the participation. According to the French law, the National Committee on Health Research Data Analysis (CCTIRS, Comité Consultatif sur le Traitement de l’Information en matière de Recherche dans le domaine de la Santé, Nimes France, file number: 11.140) and the National Committee on Information Technology (Commission Nationale de l’Informatique et des Libertés, Paris, France, file number EGY/FLR/AR114292) also approved this study. This prospective, multicenter, observational study was conducted by a French anesthesia and intensive care research network (AzuRea group). Patients were enrolled in 19 medical or surgical ICU of eight French teaching hospitals more than an 11-month period (February to December 2011). Data were anonymously collected using electronic case report form.

Brain-dead Organ Donors

All BD patients in whom organ retrieval was performed were eligible. Clinical diagnosis of BD was performed with a strict adherence to the standard international criteria and confirmed by either computed tomography angiography or electroencephalography, according to the French law. An interview of relatives and/or closest was systematically performed to confirm the absence of known refusal of the BD patients to organ donation; we also checked the French national registry of refusal of organ donation. Standard medical contraindications to organ donation were also checked. Patients in whom a contraindication to kidney donation was identified were excluded. In BD donors, the following variables were collected: age, sex, weight, height, medical history of cardiac failure (defined as New York Heart Association 3 or 4 classes), coronary artery disease, arterial hypertension, peripheral obliterating arterial disease, tobacco consumption (more than one pack per day during 20 yr), diabetes mellitus, hyperlipidemia (defined as chronic treatment for hypercholesterolemia or hypertriglyceridemia). The ECD for kidney were defined by the following elements: age older than 60 yr, age between 50 and 60 yr and one of the following risk criteria as arterial hypertension, stroke or transient ischemic attack, diabetes mellitus, and anemia. All BD patients in whom organ retrieval was performed to confirm the absence of known refusal of the BD patients to organ donation; we also checked the French national registry of refusal of organ donation. Standard medical contraindications to organ donation were also checked. Patients in whom a contraindication to kidney donation was identified were excluded. In BD donors, the following variables were collected: age, sex, weight, height, medical history of cardiac failure (defined as New York Heart Association 3 or 4 classes), coronary artery disease, arterial hypertension, peripheral obliterating arterial disease, tobacco consumption (more than one pack per day during 20 yr), diabetes mellitus, hyperlipidemia (defined as chronic treatment for hypercholesterolemia or hypertriglyceridemia). The ECD for kidney were defined by the following elements: age older than 60 yr, age between 50 and 60 yr and one of the following risk criteria as arterial hypertension, stroke or transient ischemic attack, diabetes mellitus, and anemia.

Sample Collection and NGAL Detection

To assess the whole period at risk for AKI before kidney harvesting, a blood sample (0.25 ml) was withdrawn just before entering into the operating room. Each center was equipped with a portable biological diagnostic device allowing NGAL assay in few minutes (Triag® MeterPro Meter; Biosite Inc., San Diego, CA). The NGAL measurements were performed.
by fluorescence immunoassay specific kits (Triage®, meter NGAL test, Alere, Jouy en Josas, France). The range of quantification was 60 to 1,300 ng/ml. For this technique, the reported variation coefficient was 10 to 15%.

**Kidney Recipients**

Assessment of renal function in kidney recipients was based on data obtained from the different transplantation units during the first postgraft week. DGF was the primary endpoint and was defined as any RRT before day 8 (D8) post-transplantation.24 The secondary endpoint was the failure to return to a normal graft function. A normal graft function was defined as urine output greater than 1,000 ml/day and serum creatinine less than 167 μmol/l during 2 consecutive days at D8 posttransplantation.12,25 We also recorded cold ischemic time defined as the time from aortic clamping in donor and graft declamping in recipient for each transplanted kidney.

**Statistical Analysis**

All statistical analyses were performed using SAS® (SAS Institute, Cary, NC) version 9.3. Quantitative variables were expressed as median with 25th and 75th percentiles and compared using Mann–Whitney tests. Qualitative variables were expressed as proportions and compared using chi-square tests (or Fisher exact tests when appropriate). Receiver operator characteristic curves were generated to evaluate the capacity of NGAL to predict DGF and failure to return to a normal graft function. A logistic mixed model with three hierarchical levels was used with a center random effect and a donor random effect within each center to take into account the link between the two transplanted kidneys from the same donor. Univariate and multivariate analyses were successively performed to assess the capacity of NGAL to predict DGF by adjusting on other expected predictors such as cold ischemic time, ECD, serum creatinine.

The sample size calculation was based on a previous study conducted by our group in which we found a proportion of DFG of 30%.26 We tested the hypothesis that NGAL is a significant predictor of dialysis before D8 posttransplantation, that is, that it could predict RRT with a value of area under the receiver operator characteristic curve of 0.82 and accuracy precision of 0.07 (keeping the lower value of the CI > 0.75).27 We calculated that 132 patients were required, to be conservative we decided thus to enroll at least 150 patients.

All P values were two tailed and a P value less than 0.05 was considered significant.

**Results**

During the study period, 159 BD patients with renal donation were included. Characteristics of BD patients and their management are shown in table 1. Figure 1 shows study flow chart. Dosage of S-NGAL was not performed for 13 patients leading to 146 analyzable BD donors that could have theoretically led to 292 renal transplantsations (fig. 1). Finally, 29 transplants were not grafted and 20 recipients were not assessed for renal function at D8, for a total of 243 transplants assessable for primary and secondary endpoints. The mean cold ischemic time in recipient population was 14.5 (12 to 19) h.

Among 243 recipients (115 and 128 right and left transplants, respectively), 56 (23%) needed RRT before D8 after graft. The median S-NGAL value was similar in case of RRT requirement or not (103 [60 to 300] vs. 102 [60 to 260] ng/ml, P = 0.94). The distribution of S-NGAL values was strictly comparable in case of DGF as compared to those without DGF (fig. 2A). The AUC of S-NGAL for predicting RRT in recipients was 0.50 (95% CI, 0.42 to 0.59) (fig. 2B). The AUC of serum creatinine measured at the same time was 0.60 (95% CI, 0.53 to 0.67). At D8, multivariate analysis showed that S-NGAL was not significantly associated to DGF, whereas a 1-h longer cold ischemic time and a 10 μmol/l increase in creatinine plasma value were both significantly associated to DGF (table 2).

Among the 243 recipients, 112 (46%) failed to return to a normal graft function at D8. The S-NGAL dosage were similar in case of normal graft function or not (102 [60 to 226] vs. 106.5 [60 to 317.5] ng/ml, P = 0.69). The distribution of S-NGAL values between recipients with normal graft function or not was similar (fig. 3A). The AUC the receiver operator characteristic curve of NGAL for predicting the failure to return to a normal graft function at D8 was 0.51 (95% CI, 0.44 to 0.59) (fig. 3B). In the logistic mixed model, S-NGAL was not predictive of failure to return to a normal graft function, whereas a longer cold ischemic time and an increase in creatinine plasma value were both significantly predictive of failure to return to a normal graft function at D8 (table 3).

For the need of RRT at day 8, the logistic mixed model showed no significant impact center effect (P = 0.17) or no significant impact of the link between the two transplanted kidneys from the same donor (P = 0.29). For the return to normal renal function at day 8, the logistic mixed model showed no significant impact center effect (P = 0.26) or no significant impact of the link between the two transplanted kidneys from the same donor (P = 0.06).

**Discussion**

In the current prospective multicenter study, NGAL measurement in BD organ donors failed to predict DGF or normal graft function in kidney recipients. Cold ischemic time and an increase in serum creatinine in BD donor were significantly associated to DGF.

NGAL is one of the most promising and studied AKI biomarkers.15,28 In healthy subjects, proximal and distal tubular epithelial cells synthesize and secrete low levels of NGAL that are detectable in plasma. An extra-renal production of NGAL (gut, bone marrow, and lungs) also participates to NGAL plasma level. In the glomerulus, plasma NGAL is rapidly filtered. The filtered NGAL is largely...
reabsorbed by proximal tubule, via receptor binding (Mega-lin) and endocytosis. Therefore, in physiological conditions, NGAL is barely detectable in urine or plasma. In case of AKI with acute tubular injury, plasma and urine levels of NGAL rapidly and markedly increase. This major and early response (within few hours) is of particular interest to early detect and prevent AKI. In children scheduled for cardiac surgery, the AUC for NGAL at 2 and 4 h postbypass were 0.99 and 1.0, respectively.29 In a study involving 88 general ICU patients, Constantin et al. showed that plasma NGAL increases 48 h before Risk, Injury, Failure, Loss, End-stage kidney disease criteria. In this study, a cutoff of 155 nmol/l showed a sensitivity and specificity to predict AKI of 82 and 97%, respectively, with an AUC of 0.92 (95% CI, 0.85 to 0.97). These results were weakened by less conclusive findings in adult cardiac surgery, ICU, and emergency patients, in whom AUC for S-NGAL or U-NGAL varied from 0.54 to 0.79, which can be considered as moderately informative.30–36 The main concern of NGAL interpretation in these large studies is that there is a wide overlap of NGAL values between AKI and non-AKI patients. Although a very low value (<200 nmol/l) is usually associated with no AKI, a higher value can be recorded both in AKI and non-AKI patients (false positive), especially in patients with a high

### Table 1. Characteristics of Brain-dead Donors (n = 159)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>59 (37%)</td>
</tr>
<tr>
<td>Men</td>
<td>100 (63%)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>53 (38–62)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>72 (63–81)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172 (165–179)</td>
</tr>
</tbody>
</table>

#### Medical history

- Chronic cardiac failure or coronary artery disease (missing data = 3): 11 (7%)
- Hypertension: 37 (23%)
- Peripheral vascular occlusive arteriopathy (missing data = 3): 2 (1%)
- Diabetes mellitus: 13 (8%)
- Dyslipidemia: 15 (9%)
- Smoker: 46 (29%)

#### Cause of brain death

- Stroke: 84 (53%)
- Traumatic brain injury: 57 (36%)
- Cardiac arrest: 12 (8%)
- Others: 6 (4%)

#### SOFA score

- Maximal creatinine in the last 48h before operating room (μmol/l): 90 (68–115)
- Maximal urea in the last 48h before operating room (mmol/l): 6.0 (4.7–8.4)
- Urine output in the last 12h before operating room (ml kg⁻¹ h⁻¹): 1,700 (1,100–2,500)
- Urine output in the last 6h before operating room (ml kg⁻¹ h⁻¹): 775 (485–1,200)

#### Vasovagal drugs (missing data = 11)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>145 (98%)</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>15 (10%)</td>
</tr>
<tr>
<td>Dopamine</td>
<td>7 (5%)</td>
</tr>
<tr>
<td>Terlipressine</td>
<td>2 (1%)</td>
</tr>
</tbody>
</table>

#### SOFA parameters

- Time from ICU admission to brain death diagnosis (days): 2 (1–3)
- Time from brain death to aorta clamping (h): 14 (10–17)
- Blood lactates at time of operating room (mmol/l): 1.6 (1.1–2.2)
- Heart rate (beats/min): 94 (82–112)
- Minimal mean arterial pressure in the last 24h before operating room (mmHg): 66 (60–74)
- Mean arterial pressure just before the transfer to operating room (mmHg): 85 (76–96)
- Norepinephrine posology before the transfer to operating room (mg/h): 1.78 (1.00–3.6)
- Arterial pH before the transfer to operating room: 7.40 (7.30–7.44)
- Arterial P0₂ before the transfer to operating room (mmHg): 309 (177–398)
- Arterial PCO₂ before the transfer to operating room (mmHg): 37 (32–44)
- Proteinuria before the transfer to operating room (g/l): 0.20 (0.10–0.52)
- Crystalloids in the last 24h before operating room: 3,000 (2,000–4,000)
- Colloids in the last 24h before operating room: 500 (0–1,000)
- NGAL (ng/ml) (13 missing data): 108.5 (60.0–285.0)

Results are expressed as n (%) or median (25th percentile–75th percentile).

ICU = intensive care unit; NGAL = neutrophil gelatinase-associated lipocalin; SOFA = Sequential Organ Failure Assessment.
Donor NGAL and Delayed Graft Function in Recipient

Anesthesiology 2015; 122:96-105

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negative results. Second, it has been widely demonstrated that an aggressive management of BD donor increases the number and the quality of grafts.⁶ Therefore, it can be hypothesized that a high quality of ICU care may limit AKI in BD donors. In our study, the median S-NGAL was very low: 108.5 ng/ml. Such low NGAL levels can be due to the efficacy of an aggressive donor resuscitation leading to a low proportion of significant AKI in our donors. Also, low levels of serum creatinine at the same time (table 1) confirm this hypothesis. It should also be noted that the S-NGAL values reported by Hollmen et al.²² in a similar setting were also relatively low (median = 212 ng/ml). This reinforces the idea that AKI is nowadays well controlled by aggressive donor resuscitation. As the timing of S-NGAL measurement was performed earlier in the Hollmen et al.²² study and because the median S-NGAL value was twice the value observed in the current study (212 vs. 108.5 ng/ml), it can be hypothesized that S-NGAL value decreases over time as a consequence of efficient donor management. It could also be hypothesized that serial measurement of NGAL (at admission and before surgery) could have been more informative, but the current result do not allow supporting this hypothesis. It could be interesting to test the ability of NGAL variations over time in donors to predict DGF in recipients. Third, the major factors leading to DGF might be postrecovery factors rather than factors related to pregraft donor conditions. In the current study, the multivariate analysis shows that cold ischemic time has the highest OR (tables 2 and 3), suggesting that postrecovery conditions are major determinant of graft function. Recently, Malinoski et al.³⁸ showed that age, cold ischemic time, and creatinine are independent factors of DGF. Finally, the weak prediction of DGF by S-NGAL observed in the current study (212 vs. 108.5 ng/ml), it can be hypothesized that S-NGAL is less specific than factors related to pregraft donor conditions. First, in this multicenter trial, there was no recommended donor algorithm management, especially indications for RRT. Thus, we cannot exclude that high U-NGAL concentration may also reflect extra-renal overproduction of NGAL. However, because we observed low values of NGAL in BD patients, the hypothesis that extra-renal S-NGAL production may interfere with its diagnostic accuracy is not likely.

The following limitations have to be considered to assess the clinical relevance of our results. First, in this multicenter trial, there was no recommended donor algorithm management, especially indications for RRT. Thus, we cannot exclude management heterogeneity between the different units leading to a less powerful interest of NGAL measurement. The systemic inflammatory response syndrome, which is usually observed during BD.³⁷ In the frame of renal transplantation, NGAL measurement after transplantation was suggested to be useful to follow transplanted patients and to predict graft recovery or failure.²⁰ Therefore, the usefulness of NGAL in the setting of kidney transplantation from BD donor is challenged. In the frame of BD donor, only one study tested the ability of NGAL to predict DGF.²² In this study, neither S-NGAL nor U-NGAL in donor could accurately predict DGF in recipients. This previous study had several limitations: monocentric study, measurement of S-NGAL performed before the occurrence of BD in 36% of cases and systematic use of glucocorticoids. The design of the current study ruled out this methodological limitations and showed similar results.

Several hypotheses can be raised to explain our negative results concerning NGAL as biomarker predictive for DGF that markedly differ to other clinical situations in critically ill patients. First, we decided to perform NGAL measurement at the time of surgery to detect an occult renal dysfunction after the occurrence of BD and hemodynamic stabilization. However, Hollmen et al.²² performed NGAL measurement earlier and they also failed to observe positive results. Thus, the timing does not appear as a valuable explanation for our

Fig. 1. Study flow chart. DGF = delayed graft function; RRT = renal replacement therapy; S-NGAL = serum neutrophil gelatinase-associated lipocalin.

systemic inflammatory response syndrome induced by BD, as NGAL is an acute phase protein, which depends on cytokine release.¹⁶ As S-NGAL is filtered through the glomerulus, one cannot exclude that high U-NGAL concentration may also reflect extra-renal overproduction of NGAL. However, because we observed low values of NGAL in BD patients, the hypothesis that extra-renal S-NGAL production may interfere with its diagnostic accuracy is not likely.

The following limitations have to be considered to assess the clinical relevance of our results. First, in this multicenter trial, there was no recommended donor algorithm management, especially indications for RRT. Thus, we cannot exclude management heterogeneity between the different units leading to a less powerful interest of NGAL measurement. The

159 brain-dead donors
- Paris Pitié Salpêtrière 16
- Montpellier Lapeyronie 17
- Montpellier Guì de Chauliac 35
- Clichy Beaujon 7
- Nice Saint Roch 43
- Marseille Timone 13
- Saint Etienne 13
- Nîmes 15

13 brain-dead donors with missing S-NGAL dosage

146 brain-dead donors

No graft for technical reasons
- Left kidney, n = 13
- Right kidney, n = 16

No available DGF at day 8
- Left kidney, n = 5
- Right kidney, n = 15

243 transplanted kidneys
- Left = 128
- Right = 115

• 53 (23%) recipients with RRT before day 8
• 131 (54%) recipients with normal graft function at day 8
**Fig. 2.** (A) Distribution of serum neutrophil gelatinase-associated lipocalin (S-NGAL) values obtained from donors with no subsequent renal replacement therapy (RRT) in recipients at day 8 (red dashed line) and from donors with subsequent RRT in recipients at day 8 (blue solid line). The density function represents the number of patients with a given value of NGAL. (B) Receiver operator characteristic (ROC) curve for S-NGAL to predict the need for renal replacement therapy at day 8 postgraft. The area under the ROC curve was 0.50 (95% CI, 0.42 to 0.59). No cutoff value could be identified.

**Table 2.** Donors and Transplantation Factors that Influence the Requirement for Renal Replacement Therapy in Recipients in Univariate and Multivariate Logistic Mixed Model Analyses

<table>
<thead>
<tr>
<th>Factor</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>NGAL increase &gt;1 ng/ml</td>
<td>1.001 (0.999–1.002)</td>
<td>0.48</td>
</tr>
<tr>
<td>Cold ischemic time (per increase = 1 h)</td>
<td>1.115 (1.057–1.177)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum creatinine increase in donor &gt;10 μmol/l</td>
<td>1.064 (1.006–1.126)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

NGAL = neutrophil gelatinase-associated lipocalin; OR = odds ratio.
current data show a trend for a center effect for slow graft function then we cannot reject the hypothesis that this study is underpowered to show a significant center effect. Second, we did not analyze recipient characteristics, especially age, warm ischemia time during transplantation, and severity scores. This lack of recipient's data theoretically limits the introduction of confounding variables in the model. Therefore, the current results need to be interpreted with caution.

Despite these limitations, DGF percentage is comparable to literature and usual predicting factors for DGF were also found. Then, the current population probably reflects a representative donor and recipient population. Moreover, because the NGAL values reported in the current study are very low (table 1), we think that the lack of link between NGAL and DGF is partly due to the lack of renal failure in donor and not because of confounding variables. Third, we did not analyze...
other relevant biomarker like cystatin C or cycle cell arrest biomarker or association of several markers that have recently been shown as promising.40 Finally, it could be objected that only terminal creatinine value could have been studied, rather than creatinine variation. The current result suggests that creatinine variation over time is a better predictor than NGAL for DGF. This finding reinforces the use of scores as Risk, Injury, Failure, Loss, End-stage kidney disease or surrogates; those are mainly based on creatinine variation, and widely recommended in ICU patients. It has been demonstrated that donor terminal creatinine is strongly associated with DGF.41,42 In the current study, we did not specifically studied final (terminal) creatinine value, but we recorded the variation of creatinine during the last 48 h of donor resuscitation. This variation was significantly associated with DGF. As we recorded creatinine value at the time of surgical procedure, this creatinine variation takes into account terminal creatinine value. Then, it can be postulated that the 10% creatinine variation reported in the current study indirectly reflect terminal creatinine value, but we did not specifically tested this hypothesis.

Conclusion

Unlike what has been previously demonstrated in ICU and emergency patients, S-NGAL measurement in BD kidney donor at the time of surgery does not predict delayed or normal graft function after transplantation.

Acknowledgments

The authors thank intensive care and organ donation teams of Clermont-Ferrand, Grenoble, Lyon, Marseille, Montpellier, Nice, Nîmes, and Paris Pitié-Salpêtrière. The authors thank Audrey Ayral, Françoise Casano, Loubna Elotmani, and Sophie Lloret (Department of Anesthesiology and Critical Care, Nîmes University Hospital, Place du Pr Robert Debré, Nîmes, France) for their substantial contribution to the current study. The authors also thank Mariella Lomma (Department of Biostatistics and Clinical Epidemiology, Nîmes University Hospital, Place du Pr Robert Debré) for reviewing English writing. To support this project, the major part of grants (30,000€) was obtained from Nîmes Teaching Hospital (Place du Pr Robert Debré, Nîmes, France). A private grant, obtained from ALERE society (ALERE France, Jouy en Josas, France), was also used to complete the NGAL dosing funding (3,000€). This society also provided dosing portable machines distributed in each participating unit.

Competing Interests

The authors declare no competing interests.

Correspondence

Address correspondence to Dr. Lefrant: Department of Anesthesiology and Critical Care, Nîmes University Hospital, Place du Pr Robert Debré, 30029 Nîmes 09, France. jean.yves.lefrant@chu-nimes.fr. Information on purchasing reprints may be found at www.anesthesiology.org or on the masthead page at the beginning of this issue. Anesthesiology's articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

References


Table 3. Donors and Transplantation Factors that Influence Failure to Return to a Normal Graft Function in Recipients in Uni- and Multivariate Logistic Mixed Model Analyses

<table>
<thead>
<tr>
<th>Factor</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>NGAL increase &gt;1 ng/ml</td>
<td>1.001 (0.999–1.003)</td>
<td>0.26</td>
</tr>
<tr>
<td>Extended criteria donor</td>
<td>1.573 (0.820–3.019)</td>
<td>0.17</td>
</tr>
<tr>
<td>Cold ischemic time increase &gt;1 h</td>
<td>1.073 (1.022–1.127)</td>
<td>0.005</td>
</tr>
<tr>
<td>Serum creatinine increase in donor &gt;10 μmol/ml</td>
<td>1.089 (1.021–1.161)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

NGAL = neutrophil gelatinase-associated lipocalin; OR = odds ratio.


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Appendix. AzuRea Group: www.azurea.org

The AzuRea group is a research network in perioperative medicine. In addition to authors who are affiliated to Azurea group, the following persons are members of this group and have participated to the current study:

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