Original Article

The Effects of Intensive Versus Routine Treatment in Patients with Acute Kidney Injury

An Explorative Randomized Controlled Study

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Summary

Background: In patients with acute kidney injury (AKI), specialized treatment—initiated in response to an early-warning system—may be beneficial compared with routine treatment.

Method: To explore effect estimators in a pilot trial (DRKS00010530), patients with AKI on regular wards of a university hospital were treated either in the usual way (control group) or more intensively (intervention group). The subjects were allotted randomly to the two treatment groups. The more intensive treatment consisted of an early warning system for a rise in the serum creatinine concentration, immediate consultation of a specialist, and the issuance of a patient kidney passport. The primary endpoint was recovery of renal function after AKI during the index hospitalization. Renal complications and process indicators were the secondary endpoints.

Results: The proportion of patients whose renal function returned to baseline after AKI was 50% in the intervention group (N = 26) and 42% in the control group (N = 26) (odds ratio 1.4, 95% confidence interval [0.5; 4.0], p = 0.58). The calculated glomerular filtration rate went down, from hospital admission to discharge, by 3 mL/min/1.73 m² (1st–3rd quartile: [6; –20]) in the intervention group and by 13 mL/min/1.73 m² in the control group (1st–3rd quartile: [0; –25]; p = 0.09). Complications of AKI such as hyperkalemia, pulmonary edema, and renal acidosis were rarer in the intervention group (15% versus 39%; p = 0.03). In the intervention group, compared with the control group, the cause of AKI was identified more frequently (27% versus 4%; p = 0.05); drugs with relevance to the kidney were discontinued more frequently (65% versus 31%; p = 0.01); and the diagnosis of AKI was more frequently documented in the patient's chart (58% versus 37%; p = 0.03).

Conclusion: Specialized consultations supported by an early warning system for AKI seem to be beneficial for patients. The findings of this pilot trial should be verified in larger-scale randomized controlled trials.

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With an incidence of 4–21%, acute kidney injury (AKI; acute kidney failure N 17.9 in the ICD classification) is one of the most frequently occurring and cost-intensive acute diseases in inpatients (1–6). Patients with AKI more frequently develop chronic renal failure (hazard ratio: 2.7 [7]) or terminal renal failure (hazard ratio: 4.8 [7]). The prevalence of chronic renal failure in Germany is estimated at around 2 million persons [8]. Cardiorenal complications, including death, chronic dialysis, decline in renal function, heart failure, and stroke, occur more frequently following AKI than after myocardial infarction (hazard ratio 1.4 [9]). In par-

ticular, undetected AKI, or delayed treatment of AKI, is an independent risk factor for increased hospital mortality (1). Extrapolating the data from cost surveys in England and Canada (10, 11), approximately € 1 billion is spent annually on the treatment of AKI and AKI-related complications in Germany.

The specialist medical societies are calling for urgent multimodal treatment, as part of which triggering factors as well as complications are promptly detected and resolved (12, 13). A specialist can be consulted for expert advice on treatment. Outpatient follow-up should be initiated. Nevertheless, there are deficits in

BOX 1

Specialist consultation for acute kidney injury

- Measures
 - Identify the cause(s) of acute kidney injury (AKI) in the clinical context
 - Achieve euvoolemia (through fluid administration or negative balance)
 - Pharmacological intervention: discontinue nephrotoxic drugs or switch to less nephrotoxic drugs of the same substance class or monitor plasma levels; adjust drug doses according to renal function
 - Optimize hemodynamics
 - Detect and treat electrolyte and acid-base disorders
 - Monitor treatment success during the index hospital stay (including serum creatinine, diuresis, weight, and fluid balance)
 - Recommendation for the medical discharge report to support intersectoral transfer of information regarding history of AKI
 - Recommendation for outpatient follow-up (including monitoring of serum creatinine and urinary protein)
 - Provide patient with AKI information leaflets and medical ID card (e.g., kidney passport [eFigure 1])

BOX 2

Secondary endpoints of the explorative randomized study

- Patient-relevant endpoints
 - Stage of acute kidney injury (AKI)
 - Change in estimated glomerular filtration rate (eGFR) between admission and discharge during the index hospital stay
 - Hyperkalemia (serum potassium >5.5 mmol/L)
 - Renal acidosis
 - Pulmonary edema
 - Initiation of acute renal replacement therapy
 - Discharge status
 - Newly diagnosed or worsened chronic renal failure
- Process indicators
 - Time required for screening, randomization, patient information, and data documentation
 - Diagnostic or therapeutic measures to treat AKI including etiology
 - Kidney ultrasound
 - Measures to regulate fluid and hemodynamic status
 - Acid-base/electrolyte levels
 - Discontinuation of nephrotoxic drugs
 - Drug adjustment to renal function
 - Documentation of AKI in patient record/medical report
 - Recommendation on outpatient co-treatment following AKI

terms of diagnosis and acute treatment. In approximately 75% of cases the diagnosis is not made, and treatment is often delayed by a matter of days. Fewer than 10% of patients receive specialist co-treatment (1, 14–16). In a survey of physicians involved in the treatment of patients with AKI at a total of 423 hospitals, nephrologists were involved in the most severe disease manifestation, i.e., AKI requiring dialysis, in only 22% of cases (17). The diagnosis of AKI can be challenging, since the diagnostic relevance of an increase in creatinine needs to be evaluated not only on the basis of two different cut-off values of creatinine concentration, but also taking into account two different time windows. This is further complicated by the often initially asymptomatic course. AKI early warning systems, in combination with specialist co-treatment if indicated, represent a possible means to support physicians in the diagnosis and treatment of AKI. A short summary of the most important effects of AKI early warning systems in randomized controlled studies can be found in *eTable 1*.

This explorative randomized controlled study evaluated the variability of effect estimates and

feasibility indicators of intensified treatment compared with routine treatment of patients with AKI.

Patients and methods

Search algorithm to detect acute kidney injury

The preliminary study and the explorative randomized study used an AKI search algorithm programmed in a hospital data system. The algorithm was based on the assessment of at least two serum creatinine levels and identified an increase according to the recommendations of the Kidney Disease Improving Global Outcomes (KDIGO) initiative (12). The algorithm also detected an increase of >50% of the previous level within a maximum of 7 days or of >0.3 mg/dL (>26.4 µmol/L) within a maximum of 2 days or of >0.5 mg/dL (>44 µmol/L) to >4.0 mg/dL (>354 µmol/L). Diuresis was not taken into account for AKI detection.

Study design

Preliminary study

In a preparatory step, the following parameters were recorded over an 8-month study period at Magdeburg

University Hospital, Magdeburg, Germany, which has 1130 inpatient beds and approximately 45 000 inpatient cases per year:

- Incidence
- Onset and resolution (date/time) of AKI
- The distribution of affected patients across specialist departments and regular units
- Status in terms of specialist consultation

Explorative randomized study

The study design and approach used in the randomized study are described in the *eBox*. The measures undertaken in the context of specialist consultations followed a standardized protocol based on the KDIGO recommendations (12). The corresponding measures are listed in *Box 1*.

Ethical evaluation and registration

The relevant ethics committee was informed in advance about the data collection to be carried out in the preliminary study; approval from the ethics committee and written patient consent were obtained for participation in the explorative randomized study (EK 171/13, EK 61/14). The randomized study was registered in the German Register of Clinical Trials (DRKS00010530).

Study population of the explorative randomized trial

Male and female patients aged 18 years or more who were treated on regular units for AKI and provided written consent were included in the study. The exclusion criteria were chronic dialysis dependence, kidney transplantation, treatment on a nephrology or intensive care unit, infection with human immunodeficiency virus (HIV) or hepatitis viruses, pregnancy, and participation in a drug or medical device trial.

Endpoints

The primary endpoint of the explorative randomized study was restoration of renal function following AKI, defined as the proportion of patients that regained baseline renal function, or as the change in estimated glomerular filtration rate (eGFR) between admission and discharge during the index hospital stay. Attainment of baseline renal function was defined as an increase in eGFR to at least 90% of baseline by the time of hospital discharge (6). The secondary endpoints were kidney-related complications and process indicators of clinical care and the time requirements of the study (*Box 2*).

Statistical analysis

The normal distribution assumption was checked using histograms. In the case of normal distribution, the mean and standard deviation were reported; otherwise, the median and the distance between the 1st and 3rd quartiles were given. Student's t-test was used for parametric two-group comparisons and the Mann–Whitney U test for non-parametric two-group comparisons. The chi-squared test was used for dichotomous variables and Fisher's exact test for two-group comparisons.

FIGURE 1

Flow diagram for patients in the randomized pilot study

AKI: Acute kidney injury

*1 According to the recommendations of the Kidney Disease Improving Global Outcomes (KDIGO) initiative (12), including a serum creatinine increase >50% of the previous level within a maximum of 7 days or of >0.3 mg/dL (>26.4 µmol/L) within a maximum of 2 days or of >0.5 mg/dL (>44 µmol/L) to >4.0 mg/dL (>354 µmol/L)

*2 Specialist consultation measures for AKI in *Box 1*

Since this was an explorative study, p-values were used as descriptive p-values and not adjusted for multiplicity.

Results

Preliminary study

Over the course of the preliminary study, 30 367 patients received inpatient treatment. The incidence of AKI was 4.2% (1267/30 367 patients). Around half of the AKI patients (49.6%) were treated on regular units (*eTable 2*). The highest number of these were treated in specialist surgical departments (42.0%), followed by internal medicine (36.7%) and specialist neurology

FIGURE 2

Primary endpoint: renal function recovery

a) Proportion of patients that regained their baseline renal function (odds ratio with control group as reference: 1.4; 95% confidence interval: [0.5; 4.0]; $p < 0.58$)

b) Change in renal function from hospital admission to hospital discharge (outliers included in statistical analysis; $p = 0.09$)

eGFR: Estimated glomerular filtration rate

departments (9.5%) (*eFigure 2a*). In over 85% of patients, the diagnostically indicative rise in serum creatinine occurred between 8 am and 3 pm (*eFigure 2b*). On regular units, specialist consultation was requested in 8.4% of cases (53/629). Requests for specialist consultation were made on average 2.8 days after the diagnostically indicative rise in serum creatinine concentration.

Explorative randomized study: patient flow and characterization

The AKI early warning system detected 96 patients with a diagnostic increase in serum creatinine (*Figure 1*). After excluding 44 patients, 52 patients with AKI were included. The study groups were comparable in terms of demography, comorbidities, admitting specialist department, status on admission, renal function at time of hospital admission, AKI stage, and

range of triggering factors (*eTable 3*). The average time required for screening, randomization, and patient information was 28.7 ± 3.7 min. Data documentation was completed in 147.9 ± 32.9 min per patient.

Explorative randomized study: course of renal function

In all, 50% of patients in the intervention group and 42% of patients in the control group regained their baseline renal function (odds ratio with control group as reference: 1.4; 95% confidence interval [0.5; 4.0], $p = 0.58$) (*Figure 2a*). From hospital admission to discharge, eGFR fell by $-3 \text{ mL/min/1.73 m}^2$ (1st–3rd quartile: [6; -20]) in the intervention group and by $-13 \text{ mL/min/1.73 m}^2$ (1st–3rd quartile: [0; -25]; $p = 0.09$) in the control group (*Figure 2b*). AKI-related complications such as hyperkalemia, pulmonary edema, and renal acidosis occurred less frequently in the intervention group than in the control group ($p = 0.03$) (*Figure 3*), with this group difference being due mainly to the higher incidence of hyperkalemia in the control group (*Table*). Patients with AKI-related complications had stage-1 AKI in half of the cases (*Table*). Three of 11 patients (27.3%) in the intervention group and three of eight patients (37.5%) in the control group developed newly diagnosed chronic renal failure or worsening of previously known chronic renal failure within 1 year of AKI ($p > 0.99$). Seven patients in each of the two study groups were admitted as inpatients within 30 days of discharge. Here, recurrence of AKI was seen in no patients of the intervention group and in four patients of the control group (*Table*).

Explorative randomized study: documentation and measures

Patients in the intervention group received prompt specialist consultation more frequently than those in the control group (65% versus 4%, $p < 0.001$) (*eTable 3*). The median time of consultation was the day of AKI onset in the intervention group and 2 days following AKI onset in the control group ($p = 0.003$) (*eTable 3*). The diagnosis of AKI was noted more frequently in the records of patients receiving intensified treatment than for those receiving routine treatment (*Figure 2*). Triggering factors for AKI remained undocumented and untreated less often in the intervention group than in the control group (4% versus 27%, $p = 0.05$).

In the intervention group, non-steroidal anti-inflammatory drugs (NSAID) were discontinued more frequently and renin–angiotensin–aldosterone system inhibitors suspended more often than in the control group (*Figure 2*). The recommendation for specialist outpatient follow-up was made in 13.6% of patients receiving intensified treatment, but in none of the patients receiving routine treatment (*Table*). There were no differences between the two groups in terms of documentation of diuresis and body weight, AKI diagnosis in the medical discharge report, AKI coding (ICD N17.9x), or the recommendation for primary care monitoring of renal function.

Discussion

Following a retrospective preliminary study, patients with AKI treated on regular units were randomly assigned to receive either intensified treatment or routine treatment. The preliminary study found relevant patient numbers and endpoints, as well as a balanced distribution of patients across regular units in relation to the total number of patients treated. AKI onset predominantly occurred during core working hours and a specialist consultation was rarely requested.

The randomized study groups appeared to be patient cohorts of similar structure. Specialist consultations took place in the intervention group significantly more often, and 2 days earlier, than in the control group.

The proportion of patients that regained their baseline renal function was 50% and 42% for intensified and routine treatment, respectively. From hospital admission to discharge, eGFR fell in the intervention group by $-3 \text{ mL/min/1.73 m}^2$ and in the control group by $-13 \text{ mL/min/1.73 m}^2$. Drugs were adjusted more frequently and AKI-related complications seen less often in patients in the intervention group than in the control group: in addition, causes of AKI were less likely to remain undocumented with intensified treatment. The diagnosis of acute renal injury was documented more frequently in patient records in the intervention group than in the control group. Cross-sectoral communication about AKI was suboptimal in both study groups.

A non-randomized study conducted in the USA without AKI early warning systems showed that AKI was less likely to progress to moderate or severe stages if specialist support was provided (3.3%) than with routine treatment (12.9%) (18). A systematic review found a higher number of nephroprotective measures in non-randomized original studies in which AKI early warning systems were linked to clinical action (2). A randomized study without treatment recommendations found no effects for an AKI early warning system, but demonstrated pronounced treatment deficits, including continuation of NSAID administration in patients with AKI (19). A Korean non-randomized quality assurance study reported a higher rate of renal function recovery in patients whose management included an AKI early warning system and thus the associated specialist co-treatment (20). A stepped-wedge cluster-randomized study conducted in the UK found hospital stays to be reduced by approximately 1 day for AKI patients when the AKI early warning system was combined with a reference to a bundle of clinical measures (21).

Recent publications have provided epidemiological data, described and quantified the treatment deficit, and proposed solutions (2, 16, 17). Information on the feasibility and potential effects of the intensified co-treatment of patients with AKI—triggered by an AKI early warning system—is not available for the German-speaking countries. Recent clinical studies showing proof of effect for a specialist intervention

FIGURE 3

Secondary endpoints:

AKI early warning system with intensive treatment compared to routine treatment
 AKI: acute kidney injury; NSAID: non-steroidal anti-inflammatory drugs;
 RAAS: renin-angiotensin-aldosterone system

were not randomized (18, 20), did not use an AKI early warning system (18), or did not carry out any specialist co-treatment (19, 21, 22). No randomized study has reported the occurrence of complications related to AKI or the long-term development of renal function.

To our knowledge, the present explorative study, conducted using a randomized design, is the first to investigate the effects of an AKI early warning system and prompt specialist co-treatment of patients on a regular unit. We focused on identifying feasibility indicators and on obtaining data on the variability as well as the frequency and distribution of patient-relevant effect estimates. Due to structural differences in healthcare systems, it is important to have data on treatment outcomes for AKI in the German-speaking countries.

In agreement with the lower limit of around 4% reported in the literature on AKI incidence (4), AKI was diagnosed at a rate of approximately 15–20 patients per week on regular units during the preliminary study and the randomized study. In more than 85% of cases, AKI onset occurred during core working hours, and specialist co-treatment took place as part of routine care in less than 10% of cases. Thus, intensified treatment appears to be possible at comparable hospitals. At hospitals without a specialist nephrology department, intensified co-treatment can be guaranteed at least to a certain extent by means of a care bundle stored in the hospital's information system and triggered by an AKI early warning system, as well as by continuous training (23, 24).

TABLE

Secondary endpoints: measures, course, and documentation

	Intensified treatment (N = 26)	Routine treatment (N = 26)	p
Measures			
Analysis of acid–base status, n	9 (34.6%)	8 (26.9%)	0.77
Kidney ultrasound, n	14 (53.8%)	15 (57.7%)	0.78
NSAID administration after AKI diagnosis, n	3 (11.5%)	6 (23.1%)	0.47
Suspension of RAAS inhibitors after AKI, n	9/16 (56.3%)	4/16 (25.0%)	0.07
Renal and clinical course			
Renal function (eGFR, mL/min/1.73m ² , median, 1st–3rd quartile)			
At hospital admission	52 (37–88)	59 (46–86)	0.62
At hospital discharge	49 (36–77)	45 (36–56)	0.47
Acute renal complications	4 (15.4%)	10 (38.5%)	0.03
Renal acidosis, n	3 (11.5%)	4 (15.4%)	0.69
Hyperkalemia, n	0 (0%)	4 (15.4%)	0.04
Pulmonary edema, n	2 (7.7%)	3 (11.5%)	0.66
Acute renal complications by AKI stage	4	10	0.99
Stage 1, n	2 (50.0%)	5 (50.0%)	
Stage 2, n	1 (25.0%)	2 (20.0%)	
Stage 3, n	1 (25.0%)	3 (30.0%)	
AKI duration (days, median, 1st–3rd quartile)	3.5 (2–6)	4 (3–7.3)	0.27
Acute renal replacement therapy, n	1 (3.9%)	2 (7.7%)	> 0.99
Rehospitalization within 30 days of discharge, n	7/22 (31.8%)	7/25 (28.0%)	0.78
AKI during rehospitalization, n	0/7 (0%)	4/7 (57.1%)	0.07
Deceased within 1 year after AKI, n	5 (19.2%)	4 (15.4%)	> 0.99
Hospital discharge			
To own home, n	17 (65.4%)	18 (69.2%)	0.45
To follow-up treatment, n	3 (11.5%)	5 (19.2%)	
Transfer to another hospital, n	2 (7.7%)	1 (3.9%)	
Nursing care facility, n	0 (0%)	1 (3.9%)	
Deceased, n	4 (15.4%)	1 (3.9%)	
Documentation			
Patient record			
AKI documentation, n	15 (57.7%)	7 (26.9%)	0.03
Body weight over time, n	6 (23.1%)	5 (19.2%)	0.98
Diuresis monitoring, n	12 (46.2%)	12 (46.2%)	> 0.99
Medical discharge report			
AKI in diagnosis list, n	6 (23.1%)	6 (23.1%)	> 0.99
AKI coded (N17.9x), n	9 (34.6%)	9 (34.6%)	> 0.99
Follow-up care recommendation			
Recommendation for primary care renal function monitoring*, n	2/22 (9.1%)	3/25 (12.0%)	> 0.999
Recommendation for specialist outpatient follow-up care*, n	3/22 (13.6%)	0 (0%)	0.06

* Patients who did not die during index hospital stay

AKI: Acute kidney injury; eGFR: estimated glomerular filtration rate; NSAID: non-steroidal anti-inflammatory drugs; RAAS: renin–angiotensin–aldosterone system

Taking into consideration the complementary improvement of renal endpoints, intensified treatment for AKI appears to confer a patient-relevant benefit. Given the limitations of these explorative data, no alternative explanation of the findings presents itself—with the exception of a possible α error. At a somewhat lower disease burden overall, routine treatment showed no benefit with regard to the endpoint.

This present study did not permit any conclusions at the level of statistical significance. However, the observations that baseline renal function was regained approximately 20% more often in the intensified treatment group, and that the eGFR loss was around 10 mL/min/1.73 m² lower, support clinical implications and point to the prospect of demonstrating the efficacy of the described intervention in a follow-up study with sufficient power. No comparable effects have yet been achieved in drug trials on acute or progressive renal insufficiency (25–27). On the basis of the available data, with an α error of 5% for a double-sided test and a power of 90% per group, 840 patients with AKI would be needed to demonstrate a higher proportion of patients regaining baseline renal function under intensified treatment (50%) than with routine treatment (42%). AKI-related complications are often observed as early as stage 1. This supports the call to implement measures for the prompt initiation of treatment at all stages of AKI.

The costs in terms of time, effort, and expense of specialist care in patients with AKI appear to be justified by the frequency and effects of the syndrome, and by the better treatment outcomes anticipated. Furthermore, we assume that the clinical benefit of specialist co-treatment is likely to more than compensate for the additional costs it causes. Patient kidney passports, information brochures, and measures aimed at effective cross-sectoral communication supported by the medical discharge report can serve to optimize inter-sectoral communication.

The internal validity of the results presented here is supported by the retrospective preliminary study with an epidemiological survey of AKI at the university hospital, together with the quantification of treatment gaps (16) and a review article on AKI early warning systems as a possible aid to improving diagnosis (2). On the basis of this, in the present randomized study we correctly and promptly identified and included the—even in the routine situation—heterogeneous patient collective. The randomization in this study resulted in a relatively even distribution of demographic variables and comorbidities. Data analysis ensued in blinded fashion; unblinding using the sealed randomization list occurred only after study completion. A significant intervention gradient emerged between the two study groups, since many more patients in the intervention group received prompt specialist co-treatment than in the control group. Nevertheless, these measures could not always be implemented in the intervention group, although it was not possible to determine the reasons for this in detail. It cannot be

Key Messages

- In this randomized pilot study, the proportion of patients that regained their baseline renal function following acute kidney injury (AKI) was 50% with intensified treatment and 42% with routine treatment.
- From hospital admission to discharge, the estimated glomerular filtration rate (eGFR) following AKI decreased by −3 mL/min/1.73 m² with intensified treatment and by −13 mL/min/1.73 m² with routine treatment.
- In the case of intensified treatment, kidney-relevant drug adjustments were made more often and AKI-related complications, including hyperkalemia, pulmonary edema, and renal acidosis, were prevented more frequently than with routine treatment.
- AKI was documented as a diagnosis in patient records more frequently in the context of intensified treatment than with routine treatment. The underlying causes were also more likely to be determined.
- The observed effects need to be verified in larger randomized studies.

ruled out that the nephrologist on duty prioritized a different patient-related task instead of immediately carrying out an AKI early warning system-triggered consultation (intervention group). Since AKI was documented in the patient records in only 58% of cases in the intervention group, one can assume an additional intervention effect if all cases were to be documented and consultations carried out. This randomized study had a small sample, which was oriented towards the objective of describing feasibility indicators and the variability of possible effect estimates for the purposes of conducting a randomized controlled follow-up study with sufficient power.

The therapeutic effects demonstrated in randomized studies (*eTable 1*) could be further improved upon by using a continuous AKI-prediction algorithm in real time in fully networked electronic health records, as recently presented by Tomašev et al. (28), on the basis of the primary preventive approach.

Conclusions

Within the constraints of the study limitations, the results of this explorative randomized investigation describe the feasibility and effects of specialist-supported AKI early warning systems on regular units. Studies with sufficient power are needed to demonstrate proof of efficacy for intensified treatment.

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Conflict of interest statement

PD Dr. Haase-Fielitz is editor of a book on the subject and has received honoraria from Springer-Verlag. She has received research support (third party funding) from the B. Braun Foundation Melsungen and the Dr. Werner Jackstädt Foundation Wuppertal.

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Prof. Haase is editor of a book on the subject and has received honoraria from Springer-Verlag. He has received lecture honoraria from Abbott Diagnostics.

The remaining authors declare that no conflict of interest exists.

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► Supplementary material

For eReferences please refer to:
www.aerzteblatt-international.de/ref1720

eFigures, eTables, eBoxes:
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Supplementary material to:

The Effects of Intensive Versus Routine Treatment in Patients with Acute Kidney Injury

An Explorative Randomized Controlled Study

by Anja Haase-Fielitz, Saban Elitok, Martin Schostak, Martin Ernst, Berend Isermann, Christian Albert, Bernt-Peter Robra, Andreas Kribben, and Michael Haase

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Front (folding)

„NIERENPASS“ Behandlungsausweis
Zur Ihrer erhöhten Behandlungssicherheit empfehlen wir Ihnen, diesen Ausweis bei allen (zahn)ärztlichen Behandlungen bei sich zu tragen*

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 3.) Fachärztin für Urologie/Facharzt für Urologie

*kdigo.org/clinical_practice_guidelines/pdf/KDIGO%20AKI%20Guideline.pdf (S. 8-10)

Back

Datum	Kreatinin mg/dl / µmol/l	eGFR ml/min	Albumin im Urin g/l	Protein im Urin g/l	Bemerkungen

Akute Nierenschädigung
 Datum: _____ Krankenhaus: _____ Ursache: _____

eFigure 1: Patient medical ID card for acute kidney injury (kidney passport)
 Inside view of ID card with information for patients not shown

eTABLE 1

Results of randomized controlled studies on inpatient early warning systems for acute kidney injury

Reference	Study design	Patients	Intervention	Primary endpoint*	Other effects
Selby et al. (2019) (21)	Multicenter stepped-wedge cluster-randomized study (the order in which participating hospitals entered the intervention phase of the study was randomized)	– N = 20 179 – All specialist departments	AKI early warning system, bundle of measures, AKI training program	Thirty-day mortality: odds ratio for intervention group 1.04; 95% confidence interval [0.91; 1.21]	Hospital stay reduced by around 1.5 days in patients of the intervention group
Wu et al. (2018) (22)	Single-center randomized study	– N = 467 (intervention) – N = 408 (control) – Cardiology and intensive care departments	AKI early warning system linked to bundle of measures (pop-up in hospital information system)	Rate of specialist consultation: 9% (intervention) versus 3.7% (control); p = 0.001	No group difference for hospital mortality
Wilson et al. (2015) (19)	Single-center single-blinded randomized study with parallel randomization	– N = 1201 (intervention) – N = 1192 (control) – All specialist departments	AKI early warning system with alert sent to unit medical staff (intern, resident, nurse practitioner) and unit pharmacist	Hospital mortality: odds ratio for intervention group 0.98; 95% confidence interval [0.86; 1.11]	No group difference in AKI treatment (fluid, aminoglycoside, and NSAID administration, urinalysis, ultrasound) and documentation of AKI

The following search terms were used for the literature search, conducted on 18 December 2019: "eAlert," "acute kidney injury," "randomized"

* Or main result

AKI: Acute kidney injury; NSAID: non-steroidal anti-inflammatory drugs

eTABLE 2

Preliminary study

Total inpatients* ¹	30 367
Patients with AKI, n	
All specialist departments	1267 (4.2%)
Regular units* ²	629 (49.7%)
– Patients with specialist consultation, n	53 (8.4%)
– Time from laboratory diagnosis of AKI* ³ to request for consultation, days	2.8 (95% CI [0; 9.5])

*¹ Over a period of 8 months at Magdeburg University Hospital

*² Excluding intensive care unit, intermediate care unit, emergency department with day unit, nephrology

*³ Serum creatinine increase according to the Kidney Disease Improving Global Outcomes (KDIGO) criteria (12)

AKI: Acute kidney injury; CI: confidence interval

eTABLE 3

Patient characteristics and intervention

	Intensified treatment (N = 26)	Routine treatment (N = 26)	p
Demography/specialist department			
Age, years (median, 1st–3rd quartile)	71 (60–77)	73 (61–80)	0.48
Sex (female), n	10 (38.5%)	8 (30.8%)	0.56
Body mass index, kg/m ²	27.8 ± 5.6	26.2 ± 4.6	0.28
Elective admission, n	9 (34.6%)	11 (42.3%)	0.78
Specialist internal medicine department, n	11 (42.3%)	10 (38.5%)	0.78
Specialist surgical department, n	15 (57.7%)	16 (61.5%)	0.78
Previous/pre-existing diseases			
Chronic renal failure*, n	11 (42.3%)	6 (23.1%)	0.14
Arterial hypertension, n	22 (84.6%)	20 (76.9%)	0.48
Type 2 diabetes, n	11 (42.3%)	6 (23.1%)	0.14
Coronary heart disease, n	9 (34.6%)	8 (30.8%)	0.77
Chronic obstructive pulmonary disease, n	3 (11.5%)	3 (11.5%)	> 0.99
Liver disease, n	10 (38.5%)	12 (46.2%)	0.58
Hyperthyroidism, n	0 (0%)	1 (3.9%)	> 0.99
Hypothyroidism, n	2 (7.7%)	2 (7.7%)	> 0.99
Cancer, n	15 (57.7%)	11 (42.3%)	0.33
Active cancer, n	7 (27.0%)	5 (19.2%)	0.82
AKI characteristics			
AKI stage (max.)			0.47
Stage 1, n	19 (73.1%)	17 (65.4%)	
Stage 2, n	5 (19.2%)	4 (15.4%)	
Stage 3, n	2 (7.7%)	5 (19.2%)	
AKI cause(s)			
Not documented, n	1 (3.9%)	7 (26.9%)	0.05
Postoperative, n	6 (23.1%)	7 (26.9%)	0.75
Hypovolemia, n	8 (30.8%)	5 (19.2%)	0.34
Nephrotoxins, n	3 (11.5%)	4 (15.4%)	> 0.99
Cardiac decompensation, n	1 (3.9%)	0 (0%)	> 0.99
Sepsis, n	5 (19.2%)	2 (7.7%)	0.42
Infection, n	5 (19.2%)	4 (15.4%)	> 0.99
Hypotension, n	3 (11.5%)	1 (3.9%)	0.61
Vasculitis with renal involvement, n	0 (0%)	1 (3.9%)	> 0.99
Hepatorenal syndrome	2 (7.7%)	1 (3.9%)	> 0.99
Number of AKI causes (median, 1st–3rd quartile)	1 (1–2)	1 (0–1)	0.07
Intervention			
Immediate specialist consultation, n	17 (65.4%)	1 (3.9%)	< 0.001
Time from AKI diagnosis to specialist consultation, days (median, 1st–3rd quartile)	0 (0–0)	2.0 (0.3–3.8)	0.003

AKI: acute kidney injury; max.: maximum; eGFR: estimated glomerular filtration rate

* At least stage 3 according to recommendations of the Kidney Disease Improving Global Outcomes (KDIGO) initiative (12)

eFIGURE 2

Findings of the preliminary study preceding the randomized pilot study

- a) Patients with acute kidney injury (AKI) on regular units: distribution over specialist departments
- b) Patients with AKI on regular units: AKI onset (time)

eBOX

Detailed description of the explorative randomized study

Study design and approach

A limited period of time for the inclusion of patients in the explorative randomized pilot study, deemed appropriate to the study objective, was agreed with the ethics committee. The study was conducted at Magdeburg University Hospital, Magdeburg, Germany, between November 2015 and December 2016, including follow-up observation of renal function. In the intervention group, an increase in serum creatinine level, the defining feature of acute kidney injury, was detected using the search algorithm described and set as an alert in the hospital information system. When an AKI patient was identified, the nephrologist on duty was sent an internal email with information on the patient's identify and unit. For patients in the intervention group, an immediate specialist consultation was scheduled. In addition, patients in the intervention group received an AKI information leaflet and an AKI medical ID card (kidney passport) during a medical information session. This provided patients with information on how to prevent AKI recurrence and document their renal function over time (*eFigure*). The control group received routine treatment, including the usual option to request a specialist consultation. The measures carried out according to the specialist consultation followed a standardized protocol, based on the recommendations of the Kidney Disease Improving Global Outcomes (KDIGO) initiative (12). These measures are described in *Box 1*. Patient-specific recommendations based on the specialist consultation were transmitted both in writing and orally to the medical service of the relevant specialist department. Patients were assigned to the intervention group or the control group using cluster-randomized allocation, alternating at 4-weekly intervals. The sequence of allocation was specified prior to the start of the study using a random number generator. Nurses, evaluators, and statisticians, but not the specialist consultation service, were blinded to the study group allocation.