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# Risk Management and Quality Assurance Parameters in One Hemodialysis Center: A Clinical and Patient Care Attitude

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## Abstract

### Introduction and Aims

In developed countries, 0.07% of population receives chronic hemodialysis. This number is expected to rise. This demand renders risk management and quality control essential for dialysis management.

Our prospective observational study presents a different approach for this issue, adding clinical and patient-care parameters to laboratory criteria.

### Patients and Methods

We examined 132 chronic hemodialysis patients: 28% female, 70.1±13.7 years of age, dialysis vintage: 5.19±2.0 years. Events recorded for a 12 month period were: shock, pulmonary edema, pericardial effusion, vascular access: failure, infection, and hemoglobin (Hb) extremities. Severity of each parameter was indicated by: need for acute definitive intervention, hospitalization, death. Data were analyzed to identify predictors of each outcome.

### Results

**Common Events:** shock (8.4%) and extreme Hb values (32.8%). Serum transferrin level, but not transferrin saturation, was associated with increased incidence of shock. The factor most strongly associated with studied outcomes is dialysis shift. Vascular access failure and pericardial effusion were both more frequently observed in patients on morning-shift. Event-related hospitalization was more frequent in patients on-morning shift and among patients with post dialysis hypertension.

### Conclusions

Dialysis shift, certain clinical, medication, inflammation-reactant and facility related factors, are quality of care measures, influencing wellbeing in chronic hemodialysis.

Keywords: Hemodialysis; Risk management; Quality assurance

## Introduction

End stage kidney disease (ESKD) is considered a world-wide epidemic, associated with chronic life-long medical interventions [1]. Despite tremendous progress in molecular immunology and hence, ongoing improvements in kidney transplantation management, chronic hemodialysis (HD) remains principal mode of renal replacement therapy. In developed countries, approximately 0.07% of the population receives chronic dialysis, and this number is expected to rise [2]. Mortality among chronic hemodialysis patients is estimated to be 10-fold that of age-matched controls [2-6]. Comprehensive risk management and quality control measures may improve outcomes in these high-risk patients. Both Kidney Disease Outcome Quality Initiative (KDOQI) and Kidney Disease Improving Global Outcome (KDIGO) addressed this mission [7]. Documenting critical events and examining their predictors is an important first step towards reducing risk in this population. Therefore, we performed this prospective observational study, having a different approach on quality of care measures in a hemodialysis unit, adding clinical and patient-care parameters to common laboratory criteria.

## Patients and methods

After obtaining the official ethics committee approval, all patients treated at the Nephrology Institute's Hemodialysis Unit at the E. Wolfson Medical Center were included in this report. Dialysis-associated unfavorable events (UE) were recorded during a period 12-month period (3.2010 – 3.1011)), and reported by medical staff at each morning update meeting, which is held daily. UE events were defined as:

• Hypovolemic shock, defined as systolic blood pressure of < 90 mmHg or drop in systolic blood pressure of > 40 mmHg

• Pulmonary edema, according to physician clinical diagnosis, proven by suitable radiologic finding.

• Pericardial effusion, diagnosed by physician, evidenced by echocardiogram.

• Vascular access: failure, infection.

• Hemoglobin extremities: >13, <10 g/dl.

Severity assessment of each UE was determined by the need for acute or definitive intervention, hospitalization or death, following the specific UE event.

Written informed consents were obtained from all our hemodialysis patients, regarding hemodialysis treatment, vascular access care, clinical assessment, laboratory blood tests and all accessory relevant examinations.

All patients had signed on an official inform consent for hemodialysis therapy, including obtaining of blood samples for biochemistry, hematology, endocrinology and serology as a routine monitoring in the unit. Based on lack of other kinds of intervention, we did not ask an additional agreement from our patients.

## Data Analysis

Data were analyzed on SPSS 21 (IBM Inc., Chicago, USA). Continuous data calculating the Pearson's or Spearman's correlation coefficient as appropriate. Nominal data are reported as frequency counts and presented as n(%). Associations between categorical variables were assessed using the chi square test, exact as appropriate. Continuous variables were compared across categories of shift using one way analysis of variance (ANOVA) followed post hoc by Bonferroni's test. The t-test for independent samples was used to compare continuous variables by dichotomous categories. Cox regression was used to model time to endpoint for each of the UE events. All tests are two-sided and considered significant at $p<0.05$.

## Results

We evaluated 132 chronic HD patients in our institution. Average age was 70.1±13.7 years, 28% females. Duration of treatment 4±0.34 hours three times a week, vascular access: arteriovenous fistula (62.6%), synthetic vascular graft (23.8%), tunneled central vein catheter (13.6%). Years in dialysis are 5.19±2 years. Demographic and clinical data associated to UE are presented in Table 1.

The main laboratory data of current HD follow-up of study- patients are summarized in Table 2.

Medications in regular use by the patients are listed in Table 3.

Table 1. Demographic, clinical characteristics and events of study patients

| | |
|---|---|
| Male/Female | 94(71.2%)/38(28.8%) |
| Age (year) | 70.1 +/- 13.7 |
| Years of HD | 5.19 +/- 2.0 |
| Pulmonary edema | 4(3.4%) |
| Vascular access failure | 8(6.6%) |
| Hb level extremities | 39(32.8%) |
| Pericarditis | 1(0.8%) |
| Shock | 10(8.4%) |
| Hospitalization due to or following UE | 4(3.4%) |
| Death due to or following UE | 0 |

(HD: Hemodialysis, Hb: Hemoglobin, UE: Unfavorable event).

Table 2. Laboratory results of study HD patients

| | |
|---|---|
| Hb (g/dl) | 11.7 ± 2.21 |
| Serum iron (mcg/dl) | 67.8 ± 40.92 |
| Ferritin (ng/ml) | 1074.89 ± 854.71 |
| Trans sat (%) | 30.6 ± 19.94 |
| Creatinine (mg/dl) | 7.2 ± 2.1 |
| Albumin (g/dl ) | 3.73 ± 0.49 |
| Cholesterol (mg/dl) | 152.9 ± 36.7 |
| Kt/V | 1.36 ± 0.28 |
| Phosphore (mg/dl) | 4.87 ± 1.49 |
| Calcium (mg/dl) | 9.02 ± 0.92 |
| K (mmol/l) | 5.0 ± 0.76 |
| PTH (pg/ml) | 229.4 ± 368.66 |
| CRP (mg/dl) | 2.63 ± 1.82 |

Trans Sat: transferrin saturation, PTH: parathormone, CRP: C reactive protein.

Table 3. Concomitant medications

| | |
|---|---|
| Calcium channel blocker | 44(33.3%) |
| Beta blocker | 58(43.9%) |
| Alpha blocker | 12(9.09%) |
| Diuretics | 38(28.8%) |
| Alpha 2 agonist | 19(14.39%) |
| directvasodilator | 2(1.5%) |
| ACE/ARB | 30(22.7%) |
| Iron IV | 109(82.6%) |
| Epo | 118(89.39%) |
| Statin | 33(25%) |
| Vitamin D (all derivatives) | 79(59.84%) |
| Phosphate binder | 83(62.87%) |
| Nitrate | 25(18.93%) |
| Anti-arrhythmic | 19(14.39%) |
| Oral antidiabetic drug | 11(8.3%) |
| Anti-allergic | 52(39.3%) |
| Anticoagulation (including heparin in dialysis) | 132(100%) |
| Anti-platelets aggregation/activation | 57 (44%) |

(Epo: erythropoietin)

Table 4 presents the cox regression of time to vascular access failure. Only close –to-significant results are listed. As can be seen, total serum cholesterol was the only significant predictor of vascular access failure: HR 0.96, 95% CI 0.93-0.99, p=0.03. This means that each 1 mg/dl increase in total cholesterol above 151.9 mg/dl is associated with a significant 4% decrease in risk of access failure. Creatinine was marginally significantly associated with reduced risk of access failure, HR 0.47, 95% CI 0.22-1.006, p=0.052. Also marginally associated with access failure were Kt/v (increasing Kt/V increased risk of access failure) and treatment with alpha blockers (use of these drugs was associated with increased risk of access failure).

Table 4. Variables effects on vascular access failure, cox regression to time

| | B | SE | Wald | df | Sig. | Exp(B) | 95% CI for Exp(B) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower | Upper |
| Creat | -.764 | .393 | 3.785 | 1 | .052 | .466 | .216 | 1.006 |
| T.Chol | -.039 | .019 | 4.373 | 1 | .037 | .961 | .927 | .998 |
| CRP | .016 | .114 | .020 | 1 | .887 | 1.016 | .813 | 1.270 |
| Kt/V | 3.604 | 2.118 | 2.897 | 1 | .089 | 36.755 | .579 | 2332.724 |
| Age | .016 | .044 | .128 | 1 | .721 | 1.016 | .932 | 1.107 |
| HD vintage | .186 | .248 | .562 | 1 | .454 | 1.204 | .741 | 1.957 |
| Sex | -.636 | .900 | .498 | 1 | .480 | .530 | .091 | 3.093 |
| Alpha blocker | 1.792 | .930 | 3.710 | 1 | .054 | 6.001 | .969 | 37.163 |

More than 7% decrease in survival was found among alpha blocker users vs non users HD patients with vascular access failure (Figure 1).

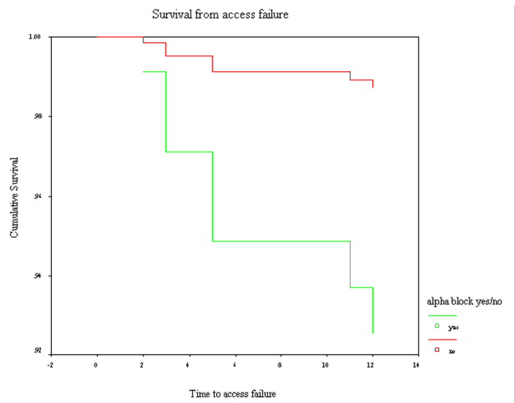



Figure 1.Survival of HD patients with vascular access failure, effect of alpha blocker

There were no significant differences in variables effects and in survival, regarding the kind of vasculer accesses (native fistula, graft, double-lumen cebtralvevous catheter).

Table 5 presents the cox regression of time to Hb extremities. Only close –to-significant results are listed. There was no significant predictor (accept from Hb itself . . .) for Hb extremities.

Post hemodialysis diastolic blood pressure (HD DBP) persists as a significant, independent predictor of hospitalization even after controlling for age, sex and dialysis vintage (Table 6): HR 0.89, 95% CI 0.79-0.99, p=0.04. Only close –to-significant data are listed.

Survival of patients with Hb extremiries was not changed by any of the variebles studied. Hb (Hemoglobin) extremities events are shown in (Figure 2). There is a fusion of all curves represented all variables, including erythropoietin and iron therapy, serum iron and transferrin saturation values.

Table 5.Variables effects on Hb extremities, cox regression to time

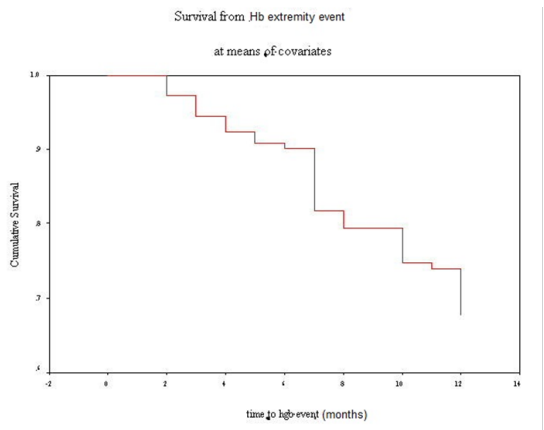
| | B | SE | Wald | df | Sig. | Exp(B) | 95% CI for Exp(B) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower | Upper |
| CRP | -.089 | .052 | 2.867 | 1 | .090 | .915 | .826 | 1.014 |
| Kt/V | .063 | .613 | .011 | 1 | .918 | 1.065 | .320 | 3.544 |
| Age | -.006 | .013 | .249 | 1 | .618 | .994 | .970 | 1.019 |
| Dialysis vintage | -.030 | .088 | .119 | 1 | .731 | .970 | .816 | 1.154 |
| Sex | .033 | .349 | .009 | 1 | .925 | 1.033 | .522 | 2.048 |
| Hb | -.227 | .080 | 8.045 | 1 | .005 | .797 | .681 | .932 |

Table 6. Variables effects on hospitalization, cox regression to time

| | B | SE | Wald | df | Sig. | Exp(B) | 95% CI for Exp(B) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower | Upper |
| HD DBP | -.118 | .058 | 4.101 | 1 | .043 | .889 | .793 | .996 |
| Age | -.012 | .046 | .070 | 1 | .791 | .988 | .902 | 1.081 |
| Sex | .509 | 1.169 | .189 | 1 | .663 | 1.663 | .168 | 16.448 |
| Dialysis vintage | .091 | .287 | .101 | 1 | .751 | 1.095 | .624 | 1.923 |

HD DBP: Post hemodialysis diastolic blood pressure

Figure 2.Survival of patients with Hb extremities




Cox regression of time to shock, transferrin emerges as a significant, independent predictor, such that each 1-unit increase in transferrin increases the risk of shock by a relative 1.6% (95% CI 1.004-1.028, p=0.011). This association persists even after controlling for age, sex, dialysis vintage, phosphate binder (Phos Bi) use and vitamin D (Vit D) use, none of which significantly predicts risk of shock. . Only close –to-significant data are listed (Table 7).

Post hemodialysis diastolic blood pressure (HD DBP) persists as a significant, independent predictor of hospitalization even after controlling for age, sex and dialysis vintage (Table 8): HR 0.89, 95% CI 0.79-0.99, p=0.04. Only close –to-significant data are listed.

Table 7. Variables effects on shock, cox regression to time

| | B | SE | Wald | df | Sig. | Exp(B) | 95% CI for Exp(B) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower | Upper |
| Vit D | 1.790 | 1.119 | 2.559 | 1 | .110 | 5.992 | .668 | 53.748 |
| Transfer-rin | .016 | .006 | 6.541 | 1 | .011 | 1.016 | 1.004 | 1.028 |
| Phos Bi | .434 | .843 | .265 | 1 | .607 | 1.543 | .296 | 8.045 |
| Sex | -.472 | .681 | .482 | 1 | .488 | .623 | .164 | 2.367 |
| Age | .008 | .024 | .123 | 1 | .726 | 1.008 | .962 | 1.057 |
| Dialysis vintage | -.061 | .179 | .117 | 1 | .732 | .941 | .663 | 1.335 |

Table 8. Variables effects on hospitalization, cox regression to time

| | B | SE | Wald | df | Sig. | Exp(B) | 95% CI for Exp(B) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower | Upper |
| HD DBP | -.118 | .058 | 4.101 | 1 | .043 | .889 | .793 | .996 |
| Age | -.012 | .046 | .070 | 1 | .791 | .988 | .902 | 1.081 |
| Sex | .509 | 1.169 | .189 | 1 | .663 | 1.663 | .168 | 16.448 |
| Dialysis vintage | .091 | .287 | .101 | 1 | .751 | 1.095 | .624 | 1.923 |

HD DBP: Post hemodialysis diastolic blood pressure

None of the continuous variables differed between patients with vs. those without an event of pulmonary edema. Post HD systolic blood pressure (SBP) and DBP were marginally lower, while pre-HD pulse was marginally higher, in subjects with vs. without pulmonary edema.

Age, dialysis vintage, transferrin saturation and ferritin differed significantly across the three shifts. In pair-wise, post hoc comparisons, we see that age was significantly older in the afternoon (AN) than the evening (E) shift. Dialysis vintage was significantly older in the morning (M) than in the AN shift. transferrin saturation and ferritin were both significantly lower in the E shift than in the M shift (Figures 3-6).

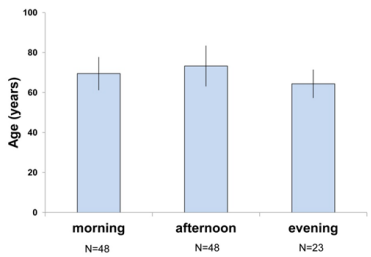



Figure 3: Difference of age by shift

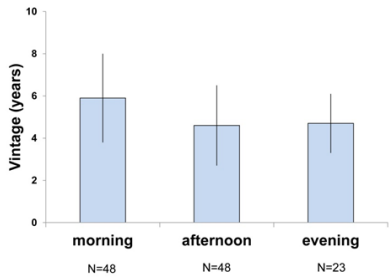



Figure 4: Difference of vintage by shift

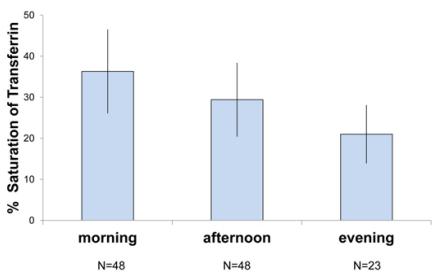



Figure 5: % Saturation of Transferrin

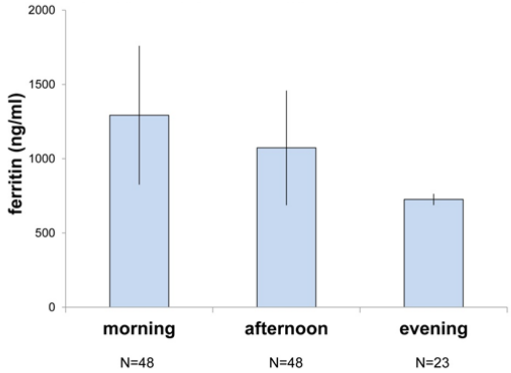



Figure 6: Difference of ferritin by shift

A significant part of patients has extremely high ferritin levels, indicating their chronic inflammatory state (mainly respiratory and vascular). Most of them are treated in the M shift, as more complicated patients. Distribution of patients between shifts: M: 48, AN: 48 and E: 23 patients.

Difference of UE prevalence in relation to treatment shifts is presented in (Table 9).

Table 9. Difference of UE by shift

| | M | AN | E |
|---|---|---|---|
| Pulmonary edema (%) | 1.7 | 0 | 1.7 |
| Vascular access failure (%) | 4.2 | 1.7 | 0.8 |
| Hb level extremities (%) | 9.2 | 17.6 | 5.9 |
| Pericarditis (%) | 0.8 | 0 | 0 |
| Shock (%) | 2.5 | 3.4 | 2.5 |
| *Hospitalization (%) | 1.7 | 0.8 | 0.8 |

M: morning shift, AN: after noon shift, E: evening shift. *Admission in hospital due to or following UE.

## Discussion

It is conventional to embed the more complicated and, sometime, critical and hemodynamically-unstable patients, in the morning full-stuffed shift. A considerable number of them are in sub-optimal nutritional state and lower serum cholesterol is one of its biochemical criteria. They are, apparently, subject to vascular access shut down or thrombotic occlusion. Furthermore, a pharmacokinetic study of alpha-adrenergic blocker, doxazosin, showed that the maximum fall in blood pressure of both healthy volunteers and patients with renal failure occurred between 4 and 8 hours. In four of five volunteers, blood pressure had returned to baseline within 10 to 12 hours, whereas patients with renal failure (four of them on hemodialysis) it took as long as 72 hours [16].

Hb extremities are the most frequent single UE occurred (in 32.8%). Its prominence in afternoon (AN) shift compared to morning (M) and especially to evening (E) shifts, may stems from difference in reporting precision. Anyhow, it is not influenced by any other variable studied. A strict monitoring of blood count, beyond the routine custom in our facility (monthly comprehensive lab survey), is quite worthwhile for minimizing the phenomenon and the risks it holds [11,14]. Serum transferrin concentration is the only variable to affect the incidence of shock during dialysis in this study. Transferrin saturation and Hb have no predicting value and therefore not related to transferrin changes in this context. Transferrin is considered a chronic inflammatory biomarker in hemodialysis. The more variability in its serum level of hemodialysis patients – the higher inflammation activity had been demonstrated [17]. In a study of cell culture, it was shown that endocytosis of transferrin, which is involved in the delivery of iron to the cell, was increased after stress induced by heat shock or after incubation with inhibitors of Hsp (heat shock protein) 90 function. It was postulated that the removal of iron from the environment is an important process to preserve cellular integrity and function [18].

These two findings, together with the present study observation, raise the possibility of transferrin as a predictor biomarker for susceptibility to hemodynamic instability including shock, when underlined chronic inflamatory state persists (as the rule in end stage kidney disease) we did not find any predicting or associated factor for pulmonary edema, among all data and events. These include the demographic and medical care methods and systems studied. This fact leads to the implicated suggestion that this UE is a result of patient-dependent background: compliance, cardiac morbidity. Its appearance was 4%, equally divided between M and E shifts. One can say that some of the evening-patients are not necessarily easy, so that they should be closely monitored and personally educated.

Among 4 hospitalized patients, one diagnosed with pericardial effusion, two suffered from pulmonary edema and one admitted after recovery from deep shock. An increased post-dialysis diastolic blood pressure is the only predicting variable for UE related hospitalization in studied patients (Ignoring the one patient with pericardial effusion).

This result is consistent with a meta-analysis of 8 studies on chronic hemodialysis (1679 patients and 495 cardiovascular events) made by an Australian group. They concluded that systolic and diastolic blood pressure lowering treatment was associated with lower risks of cardiovascular events, all-cause mortality and cardiovascular mortality than control regimens [19].

In this study, rates of UE-related are not represented the all-causes- related hospitalization and/or mortality of our patients. The latter are derived from variety of variables and factors beyond the study scope.

Impact of timing of dialysis shifts on patient outcomes have not been received much attention, compared to dialysis day and inter-dialysis interval. Dialysis day after the long interdialytic interval exhibits inordinately high mortality.

One US study examined outcomes in 6939 patients. Shift-associated mortality differences were present in patients < 60 years, with 4-year mortality risk as follows: morning shift, 28.8%; afternoon shift, 24.1%; evening shift, 38.7% [20-21].

Direct association of dialysis shift to all-cause mortality was not evaluated in this study. However, mortality and morbidity potential arguments are represented in relation to UE and demographic data of the patients on the various shifts. By this way we try to prevent possible hazardous outcomes which stem from embedding the inappropriate patient on inappropriate time shift.

In conclusion, this study completes the existent standards accepted by nephrologists, most of them leaning on laboratory-derived criteria.

The association of vascular failure to low cholesterol levels and alpha blocker medications, shock events to high serum transferrin, UE-related-hospitalization to post dialysis hypertension – are interesting results and subject to farther evaluation including larger study population. By the same token – increased incidence of vascular failure and hospitalization in M shifts and pulmonary edema in M and E shifts – can serve as arguments for considering more careful policy concerning embedding patients and professional medical stuff to customary time sifts in the dialysis unit.

## Declaration

The authors declare that there is no conflict of interests regarding the publication of this article. There are no grants and funds involved in this study.

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