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Cross-sectional Study

Predisposing factors and uremic pericardial effusion among ESRD patients undergoing dialysis☆

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ABSTRACT

Objective: Pericardial effusion and pericarditis are responsible for 3–5% of deaths due to tamponade, fatal arrhythmia and heart failure. Improvement in dialysis methods has allowed the initiation of the treatment at early stages. This study is designed to evaluate the prevalence of pericardial effusion and its predisposing factors among end-stage renal disease (ESRD) patients undergoing dialysis.

Methods: This is a cross-sectional study that included patients from the two Medical Centers in (XXX). These patients were presented with ESRD with a GFR <10 cc/min and were under long-term dialysis, also called chronic hemodialysis. The echocardiography was performed and patients with pericarditis and/or pericardial effusion due to non-uremic causes or dialysis were excluded.

Results: Of 132 patients included, mild pericardial effusion was observed in 17(12.9%) patients, 8(6.1%) patients were presented with moderate and 1 (0.7%) had severe pericardial effusion. Among females, 9(15.8%) showed pericardial effusion whereas, it was reported in 8(10.7%) males, with no statistically significant difference. Furthermore, no significant difference was seen in the ages or etiologies of patients with or without pericardial effusion (50.5 ± 15.5 vs 52.8 ± 16.1, respectively).

Conclusion: Our study reports that echocardiography among dialysis patients is likely to determine the effectiveness of the dialysis procedure and can be a cost-effective approach. Futher studies regarding laboratory parameters are required in this area.

1. Introduction

Adverse cardiovascular events are commonly reported causes of mortality among end-stage renal disease (ESRD) patients [1,2] such as; coronary heart disease, stroke, cardiometabolic disorders, myocardial infarction [3], heart failure, ischemic heart disease, heart failure, and cardiac arrhythmia [4]. Uremic pericarditis, defined as presentation of clinical signs and symptoms before or within 8 days of renal replacement therapy [5], and is reported in 16–41% patients undergoing dialysis. Dialysis pericarditis is referred as the onset of sign and symptoms 8 weeks after renal replacement therapy, however, patients on long-term dialysis, greater than 8 weeks [6], are also at the risk of developing uremic pericarditis [5]. Furthermore, pericardial effusion can also be seen without the sign of pericarditis among these patients. Metabolic alterations such as hypocalcemia, hyperparathyroidism, hypoproteinemia, and hyperuricemia are predicted to contribute to pericardial effusion [7]. Lately, it has been established that incidence of uremic pericarditis is lowered among chronic dialysis patients, 5–20%, owing to the advancements in the dialysis procedure [8].Accumulation of toxic metabolites, high albuminuria, lowered creatinine clearance and difficulty in the maintenance of normal blood pressure during dialysis are some of the common causes of pericarditis and pericardial effusion in these patients [5]. In general, ESRD patients are presented with cardiovascular complications such as fluid overload, atherosclerosis, anemia and arteriovenous fistulas, which makes it challenging to segregate them from uremic cause [9]. The diagnosis is usually made by the means of imaging modalities such as electrocardiography, echocardiograph, chest x-ray and routine blood lab tests [5].

Abbreviations: ESRD, end-stage renal disease.

☆ This study was approved by the Research Ethics Board of Tehran University of Medical Sciences.

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The aim of this study is to provide reliable data on the prevalence of pericardial effusion and its predisposing factors among ESRD patients, undergoing long-term dialysis.

2. Materials and methods

This cross-sectional study was conducted on ESRD patients visiting (XXX) Heart Center for chronic maintenance dialysis with a GFR <10 cc/min. Echocardiography was performed on these patients. Uremic carditis was defined as the occurrence of pericardial effusion in the 8 weeks before or following the dialysis. Presence of mononuclear inflammatory cells was also confirmed through histology as indicated in previous studies [10]. We included the cases who were presented with uremic pericarditis (within 8 weeks of renal replacement therapy) only. Pericarditis cases after 8 weeks of dialysis or before dialysis were excluded. The cases with existing pericarditis and/or pericardial effusion due to non-uremic causes (sudden onset of chest pain on the anterior chest wall, that increases with the inspiration and in supine position, pericardial friction rub and changes in ST waves, seen in echocardiography [11]) including cancer, infections, injury (thoracic, esophageal and iatrogenic trauma) and patients who did not consent to participate were also excluded from the study. Written consent was obtained from all the patients and were also briefed the procedure and the purpose of the study.

Considering a 5% type I error, 0.2% prevalence of pericardial effusion, 70% study power and 95% confidence interval; the sample size was calculated at 125.

Initially, serum calcium and phosphorus concentrations and creatinine levels in both serum and urine were evaluated. Serum lipid profile, serum albumin, hormone tests such as thyroid and parathyroid along with complete blood count were also analyzed. All biochemical measurements were performed using enzymatic techniques by "Pars Azmoon Kits" manufactured in Iran, while hormone-related tests were performed via immunoassay using "Immunotech Kits", made in Czech Republic.

Hemodialysis (vascular access) was performed without anticoagulation and an ultrafiltration rate <800 ml/h was used along with dialysate Na + concentration of 138 mEq/L.

After 8 weeks of last session of dialysis, echocardiography was performed by cardiologists using SIMS 7000 Toshiba (Japan). This was to analyze the presence or absence of pericardial effusion as well as its severity and volume. The severity was defined as small (10 < mm echo-free space behind the left Ventricle); moderate (10–20 mm, echo-free spaces behind the left ventricle and in front of the right ventricle in less than 1 cm) and large (>20 mm which was the mentioned finding in addition to a right-sided atrial collapse).

The data were evaluated using SPSS 12. Mean and standard deviation were used for the expression of continuous parameters. The two groups of the patients, with or without pericardial effusion, were compared in the form of percentages using chi-square test where p-value < 0.05 was considered significant. The calculated means were then compared by an independent *t*-test or Mann–Whitney *U* test. Logistic regression was used for multivariate analyses. This study was approved by the Research Ethics Board of (XXX). All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Unique identifying number is: researchregistry7625.

The methods are stated in accordance with STROCSS guidelines [12].

3. Results

A total of 132 patients was included with 75 males (56.8%) and 57 females (43.2%) presenting the mean age of 52 ± 16 years. Diabetes mellitus was the etiology of ESRD in 42 (31.8%) cases, while 29(22%) had a history of hypertension before ESRD, summarized in Table 1.

Pericardial effusion was observed in 17(12.9%) patients where it was mild in 8(6.1%), moderate in 8(6.1%) and large in 1 (0.7%) case(s). Among females, 9(15.8%) showed pericardial effusion whereas, 8 (10.7%) males had pericardial effusion There was no significant difference in the mean ages 50.5 ± 15.5 vs 52.8 ± 16.1, respectively) and the etiologies of the patients with and without pericardial effusion. Serum BUN, creatinine, calcium and phosphorus were statistically different in patients presenting pericardial effusion, indicated in Table 2. Using a multivariable logistic regression test, the independent statistical correlation between the four mentioned parameters and pericardial effusion was noted, p = 0.029, p = 0.017, p = 0.02 and p = 0.03.

Concerning the mean dialysis period, the patients with pericardial effusion had suffered the procedure for 17.5 ± 8 months compared to the other group 30.8 ± 14 months (P value = 0.057).

4. Discussion

The collection of uremic toxins is likely to be the known cause of pericarditis. Furthermore, chronic buildup of the volume and hypoalbuminemia can also lead to non-inflammatory type pericardial effusion [7]. Patients with chronic kidney disease are also presented with uremic risk factors of cardiovascular disease such as increased oxidative stress, homocysteine, and lipoproteins [13]. Among patients undergoing hemodialysis due to chronic renal failure, pericarditis is a frequent and serious complication [14]. The use of dialysis in the early stages of the renal diseases including ESRT, the prevalence of pericardial effusion and pericarditis and associated mortality have been dramatically reduced [15,16]. Furthermore, echocardiography has enabled early diagnosis of these adverse events, particularly in non-symptomatic patients [17]. Dialysis-associated pericarditis is seen in patients who are under-dialyzed and are being capable of responding to intensification of dialysis [18].

In this study, pericardial effusion was found in 13% of the patients. A study showed that among hemodialysis ESRD and chronic kidney disease patients, pericardial effusion is seen to be 14.3% [13]. However, a study by Ravi, Iskander [7] reported a relatively higher incidence of pericardial effusion among dialysis patients, 44%. In a recent retrospective study, Bentata, Hamdi [19] reported that the incidence of small, moderate and large pericardial effusion among ESRD patients were 31.2%, 37.6% and 31.2%, respectively, which was small 8(6.1%), moderate in 8(6.1%) and large in 1 (0.7%) case(s) in our study. Similarly, in another retrospective study, Bataille, Brunet [20] showed that the incidence of small, moderate and large uremic pericarditis was 38%, 32% and 30%, respectively. Serum BUN and creatinine were positively correlated to the incidence of pericardial effusion in our patients. A recent study by Ravi, Iskander [7] reported that serum BUN and creatinine are significantly greater among chronic kidney or ESRD patients presented with pericardial effusion than patients otherwise. Nonetheless, greater sample size can confirm our findings with well-adjusted variables. However, many factors such as dialysis efficacy, nutrition

Table 1
Etiology of pericardial effusion among recruited patients with ESRD.

	Pericardial effusion		
Etiology	Pos n (%)	Neg n (%)	**sum**
Diabetes mellitus	5(11.9)	37(88.1)	42(100)
Hypertension	2(6.9)	27(93.1)	29(100)
Glumeronephritis	0(0)	10(100)	10(100)
Infectious nephritis	1(12.5)	7(87.5)	8(100)
PKD	1(14.3)	6(85.7)	7(100)
Obstructive	0(0)	2(100)	2(100)
Others/Unknown	8(23.5)	26(76.5)	34(100)
Sum	17(12.9)	115(81.1)	132(100)

PKD: Polycystic kidney disease.

Table 2
Means of measured parameters among patients with or without pericardial effusion.

	Pericardial effusion		
Parameter	Pos (mean)	Neg (mean)	**P Value**
SBP(mmHg)	142 ± 22	135 ± 21	0.229
DBP(mmHg)	85 ± 11	80 ± 12	0.637
Dialysis efficacy (kt/V unit)	1.21 ± 0.36	1.15 ± 0.33	0.499
Serum BUN(mg/dl)	110 ± 41	89 ± 46	0.029[a]
Serum Cr(mg/dl)	8.9 ± 1.8	7.6 ± 2.5	0.017[a]
Hb(gr/dl)	9.5 ± 1.7	9.7 ± 2.1	0.549
Serum P(mg/dl)	5.3 ± 1.4	3.8 ± 1.2	0.02[a]
Serum Ca(mg/dl)	8.9 ± 1.1	8.4 ± 0.8	0.014[a]
Alk-P(mg/dl)	282 ± 224	248 ± 228	0.512
Serum P*Ca(mg/dl)	47.6 ± 12	36.5 ± 11	0.008[a]
Serum Albumin (gr/dl)	3.7 ± 0.45	3.7 ± 0.47	0.039[a]
Uric acid(mg/dl)	5.6 ± 1.9	6.23 ± 1.5	0.359
Cholesterol(mg/dl)	147 ± 36.8	153.9 ± 40.7	0.156
TG(mg/dl)	142 ± 55.6	141.1 ± 74.3	0.992
Serum free T4 (μg/dl)	95 ± 42.1	98.9 ± 26.3	0.506
Serum free T3 (μg/dl)	2.3 ± 1.8	2.4 ± 2.2	0.812
Parathormone(μg/dl)	342 ± 272	248 ± 244	0.217

SBP: Systolic blood pressure; **DBP:** Dyastolic blood pressure; **Hb:** Hemoglobin; **P:** Phosphorus; **Alk-P:** Alkaline phosphates; **TG:** Triglyceride.
[a] statistical significance.

status and muscular mass affect serum Cr concentration. Bataille, Brunet [20] reported that hypoalbuminemia and the size of pericardial effusion can significantly predict the requirement of the drainage in these patients. Despite our study did not presented such data, hypoalbuminemia was significant in pericardial effusion patients in our study.

5. Conclusion

This study found a significant inverse correlation between the duration of dialysis and the occurrence of pericardial effusion. Serum calcium and phosphorus are also inversely correlated with pericardial effusion, nonetheless, results from a greater sample size can lead to accurate conclusions. Dialysis patients have been reported to develop pericarditis as a result of multiple causes such as post-myocardial infarction, lupus, cancer and infections. These conditions should also be considered when evaluating uremic pericarditis or dialysis-associated pericarditis patients.

Considering mortality and morbidity resulting from pericardial effusion and pericarditis, especially in ESRD patients experiencing hemodialysis as well as similar symptoms of uremic and non-uremic pericarditis, pericardial effusion, cardiac tamponade and constrictive pericarditis, this research concludes that early echocardiography can beneficial at the time of initiation of dialysis. Normal serum BUN and Cr concentrations are not solely reliable predictors of effective hemodialysis.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethics approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent

Not applicable.

Availability of data and materials

All relevant data and materials are provided with in manuscript.

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Author contribution

Dr. Ziba Aghsaeifard: conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Rahim Firouzi: Designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript.

Dr.Reza Alizadeh: Coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

Registration of research studies

- Name of the registry: N/a.
- Unique Identifying number or registration ID:
- Hyperlink to the registration (must be publicly accessible):

Guarantor

Ziba Aghsaeifard.

Declaration of competing interest

The authors deny any conflict of interest in any terms or by any means during the study. All the fees provided by research center fund and deployed accordingly.

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