Disappearance of mitral and tricuspid regurgitation in haemodialysis patients after ultrafiltration

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Abstract

Background. Doppler echocardiography has recently revealed frequent occurrence of valvular (in particular mitral) regurgitation in dialysis (HD) patients. We hypothesized that this may be in part ‘functional’ and related to the cardiac dilatation which is also frequently present. Thus it would be possible to improve it by ultrafiltration.

Methods. Mitral and tricuspid regurgitation was detected in 21 haemodialysis patients who had cardiomegaly but no manifest cardiac failure. They were treated by intensified ultrafiltration sessions, as much as they could tolerate, while all antihypertensive drugs were stopped. Doppler echocardiograms were then repeated.

Results. Mitral regurgitation disappeared in 13 and tricuspid regurgitation in 14 patients, while lesser degrees of either of them persisted in seven. This was accompanied by decreases of body weight (5.4 ± 2.7 kg) mean arterial pressure (125 ± 15 to 95 ± 11 mmHg), cardiothoracic index (from 0.57 to 0.47), and left atrial (28 ± 4 to 22 ± 3 mm/m²), left ventricular systolic (25 ± 5 to 21 ± 55 mm/m²) and left ventricular diastolic (31 ± 5 to 27 ± 5 mm/m²), and mitral annular diameters (19.4 ± 2 to 16.6 ± 2 mm/m²). Ejection fraction increased but remained below 50% in 11 patients.

Conclusion. Most of the mitral and tricuspid regurgitations seen in HD patients are partly or completely functional, due to dilatation of the mitral annulus which is related to volume overload. A more aggressive approach, while discontinuing antihypertensive drugs can correct or improve many of them and also ameliorate cardiac function.

Key words: cardiac dilatation; haemodialysis; mitral regurgitation; tricuspid regurgitation; ultrafiltration

Introduction

Valvular regurgitation in dialysis patients is generally considered to be progressive and indicates a grave prognosis [1]. On the other hand, systolic cardiac murmurs are often present in haemodialysis patients; they may disappear with control of congestive failure and hypertension [2] and have therefore been called ‘functional’. The nature of this functional disturbance has been variously related to anaemia and high cardiac output (systolic flow murmurs) [2], duration of dialysis and disturbed calcium metabolism [3, 4], and dilatation of the left ventricle [3]. Systematic echocardiography has recently confirmed that mitral and tricuspid regurgitation are indeed frequent in renal failure patients [3, 4]. Because volume overload and cardiac dilatation is often present in these patients, we hypothesized that this may be the cause or aggravating factor in many cases. Consequently, it would be possible to improve such regurgitation by good volume control with ultrafiltration.

Subjects and methods

End-stage renal failure and dialysis patients with cardiac dilatation and hypertension are often referred to our hospital. We treat them with intensified ultrafiltration until normovolaemia is reached. An echocardiogram is sometimes taken when the cause of cardiomegaly is not quite clear. During a period of 2 years we observed mitral and tricuspid regurgitation on Doppler echo examination in 21 patients. The echocardiogram was repeated after normovolaemia was considered to be reached.

The male/female ratio of the study group was 12/9, their ages ranged from 17 to 64 years (mean 44 ± 11 years). The time on dialysis ranged from 1 to 60 months (mean 15.7 ± 15). Diagnoses were: chronic glomerulonephritis 6, interstitial nephritis (various causes) 4, diabetes 3, hypertensive nephrosclerosis 2, polycystic disease 1, and unknown 5. Urinary output varied between anuria and 800 ml/day, except in the patient who had been only 1 month on dialysis. Most of them were hypertensive but three had blood pressure (BP)
Interventions

After completion of the UF treatment, a mean MR, mitral regurgitation; TR, tricuspid regurgitation; AR, aortic regurgitation; B, before treatment; A, after treatment.

| Pat. no | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 |
|--------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|
| MR     | B | 3° | 3° | 1° | 1° | 2° | Ø | 1° | 4° | 2° | 4° | 2° | 1° | 1–2° | 1° | 1° | 2° | 1° | 2° | 2° | 2° |
| TR     | A | 1° | 1° | Ø | Ø | Ø | Ø | Ø | 1–2° | Ø | Ø | Ø | Ø | Ø | Ø | 1° | 1° | 1° | 1° | 1° | 1° | 1° |
| AR     | B | Ø | 1° | Ø | Ø | Ø | Ø | Ø | Ø | Ø | Ø | Ø | Ø | 1° | Ø | Ø | 1° | Ø | Ø | Ø | 1° |
|        | A | 1° | 2–3° | 1° | 2° | 1° | 1° |

MR, mitral regurgitation; TR, tricuspid regurgitation; AR, aortic regurgitation; B, before treatment; A, after treatment.

Results

Echocardiographic findings of mitral and tricuspid regurgitation of varying degrees were present in all patients. Two patients also had first-degree (1°) and one had second-third degree (2–3°) aortic insufficiency. Calcifications were not a prominent feature but in seven patients light calcifications of the mitral annulus were noticed and in four patients small nodular calcifications (<2–3 mm) were present on mitral valves or chordae. One patient had mitral prolapse. In 14 patients small amounts of pericardial effusion were noticed.

After completion of the UF treatment, a mean weight loss of 5.4 ± 2.7 kg was achieved. Regurgitation improved in all patients, mitral regurgitation (MR) disappeared in 13 but first-degree MR persisted in seven patients, while tricuspid regurgitation (TR) disappeared in 14 and persisted in four. Aortic insufficiencies were observed in three patients and persisted after treatment (Table 1).

Before treatment, diameters of cardiac compartments were increased in every patient and varying degrees of myocardial hypertrophy were present. Mean interventricular septum thickness was 13.1 ± 2.2 mm (range 8–17 mm) and mean posterior wall thickness was 12.6 ± 1.8 mm (range 10–17 mm).

The main results before and after treatment are given in Table 2. There were marked decreases in blood pressure when it was previously elevated. Antihypertensive drugs were not needed in any patients. Cardiac volume on the chest X-ray and diameters of cardiac compartments decreased in every patient without, however, reaching normal values in most. Mitral annular diameter decreased from 3.9 ± 0.6 to 3.2 ± 0.7 cm. All of these changes were highly significant. The largest relative changes were noted in inferior vena cava (−25%) and left atrium diameter (−24%).

Initially, left ventricular ejection fraction (EF) was slightly to markedly decreased in most patients and it increased after treatment as shown in Figure 1. However, it remained below 50% in 11 patients.

In addition, significant increases were noted for haematocrit (htc) (from 23.4 to 27.7%) and serum albumin (from 3.3 to 4.1 g).

We compared the final cardiac dimensions of the
Disappearance of valvular regurgitation in HD patients after UF

### Table 2. The main clinical findings before and after the treatment

<table>
<thead>
<tr>
<th></th>
<th>Age (year)</th>
<th>MAP (mmHg)</th>
<th>CTI %</th>
<th>LA (mm/m²)</th>
<th>MAD (mm/m²)</th>
<th>Lvs (mm/m²)</th>
<th>LVd (mm/m²)</th>
<th>VC (mm/m²)</th>
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<tbody>
<tr>
<td>B</td>
<td>48.7 ± 13</td>
<td>125 ± 15</td>
<td>57 ± 4</td>
<td>28 ± 4</td>
<td>19.4 ± 3</td>
<td>25 ± 5</td>
<td>31 ± 5</td>
<td>13 ± 2</td>
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<tr>
<td>A</td>
<td>59 ± 11</td>
<td>47 ± 4</td>
<td>22 ± 3</td>
<td>16.6 ± 2</td>
<td>21 ± 5</td>
<td>27 ± 5</td>
<td>9.6 ± 2</td>
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P1, comparison of echocardiographic values of study group before (B) and after (A) UF treatment.

MAP, mean arterial pressure; CTI, cardiothoracic index; LA, left atrial index; MAD, mitral annular diameter; Lvs, left ventricle systolic index; LVd, left ventricle diastolic index; VC, vena cava index. All differences between groups were significant (P<0.01).

Fig. 1. Individual values of EF before (■) and after (□) UF.

seven patients in whom either MR or TR persisted with the 14 patients who showed no regurgitation after treatment. No significant differences were present, although left ventricular diameters were slightly larger and ejection fraction slightly lower (NS) in the former group. Calcifications of mitral annulus or chordae were not more frequent in the group with residual regurgitation.

**Discussion**

The rather frequent occurrence of mitral regurgitation in dialysis patients is well documented in recent literature, but to our knowledge the present study is the first to document any cure or improvement following decreased cardiac dilatation by strict volume control. An angiographic study [1] performed in 77 transplantation candidates over the age of 50 with at least one risk factor revealed valvular heart disease in 22%. Among these 77 patients 13 had mitral regurgitation and/or stenosis. In nine (often severe) aortic valvular disease was present, but tricuspid regurgitation was detected in only two patients. Other clinical details were not given. Interestingly, 28 patients had a murmur without valvular disease and three had no murmur despite significant disease. More recently echocardiographic studies have confirmed that valvular regurgitation is frequently present in dialysis patients, and emphasized the association with mitral annular calcifications [3,4,10–13].

Bryg et al. [3] reported on 114 patients with end-stage renal disease. Mitral regurgitation was present in 38% (moderate to severe in 13%), and tricuspid regurgitation in the same percentage. Calcifications were seen in 44% of the former. Similar frequency was observed by Hüting [11] who stressed the association with left atrial and ventricular dilatation. He also suggested a pathogenic role for mitral annular calcifications related to calcium–phosphate disturbances, but this relationship was not confirmed by others [4,12].

Among 135 CAPD patients Fernandez-Reyes et al. [12] found mitral insufficiency in 13% at first presentation and a similar de novo appearance during follow-up. Calcifications were present in the majority. They also remarked a strong association with left atrial dilatation, which appeared prior to the insufficiency. In none of these studies was regression of regurgitation mentioned.

It may be concluded from these studies that regurgitation of the mitral valves and annular calcification are frequently associated both with and without renal disease but that the relationship between the two conditions is not clear. Increased intracardiac pressure and dilatation seems to be more important in the pathogenesis than abnormal calcium metabolism.

In our series, calcifications were less frequent (30%) than reported in the other series of mitral regurgitation, suggesting that other factors such as duration of dialysis and age are more important for the calcifications to develop. In contrast, regurgitation was apparently related to the severity of overhydration. After serial ultrafiltration sessions 14 patients were free of regurgitation while the others improved. In three patients aortic insufficiency was also present but this was not improved by the treatment as can be expected. The very marked decreases in cardiac dimensions (Table 1)
in particular of the left atrium, and of the mitral annular area strongly suggest that the improvements were due to the resolution of a functional disturbance of the mitral annulus resulting from the ultrafiltration treatment. The significant decrease of the mitral area by 14% supports this contention. The coexistence of tricuspid with mitral regurgitation in our study, as well as their disappearance after ultrafiltration, suggest a common mechanism. It is indeed known that tricuspid insufficiency is often secondary to left ventricle valvular disease [9].

The reason why some degree of regurgitation persisted in seven of the patients cannot be established with certainty. In our opinion ‘dry weight’ or ‘normovolaemia’ cannot be defined by one single criterion, and have to be established empirically. While blood pressure was normalized in all patients without the use of hypotensive drugs, diameters of left atrium and ventricle were still in the high-normal range in some of them. It thus is not excluded that they would have regressed with more ultrafiltration. However, no significant differences in this values between those with and without residual regurgitation were found. The other possibility is that some structural damage may be present. This matter is currently under investigation in our department.

The mechanism responsible for secondary mitral regurgitation has been extensively investigated by Boltwood et al. [13]. In a group of non-uraemic patients with dilated cardiomyopathy they found no significant clinical difference between those with or without regurgitation. However, the former had strikingly larger left atrial volume and mitral area index (6.3 cm²/m²) than those without (4.6 cm²/m²) while left ventricular volume was not significantly different. The authors point out that the posterolateral annulus is contiguous with the posterior wall of the left atrium, which has sparse connective tissue and is therefore more apt to be stretched by enlargement of the atrium. They therefore suggest that more severe cardiac failure may not account for the difference in atrial size but that there seems to be a ‘regurgitation threshold’ which, once passed, leads to a vicious circle: ‘mitral regurgitation begets mitral regurgitation’ [13]. This consideration is particularly relevant to dialysis patients who are continuously threatened by overhydration, stretching the most compliant part of the heart, the atrium. Our observation that ultrafiltration treatment decreases atrial diameter and greatly improves both the regurgitation and the clinical condition is in accordance with this pathogenic mechanism.

Mitral and tricuspid insufficiency in dialysis patients carries a bad prognosis and is often progressive [1,11,12]. We showed that the latter is not necessarily the case. As we did not systematically investigate all our patients when they were overhydrated, functional regurgitation may have been more frequent than appears from our study.

Our results, while not unexpected are, to the best of our knowledge, the first published. Foley et al. [14] recently emphasized that cardiac dilatation is a very strong and independent risk factor. The present study shows that valvular regurgitation may be part of such dilated cardiomyopathy but, more importantly, that meticulous volume control can partly or completely correct it, while at the same time impressive improvement of blood pressure and cardiac dimensions can be obtained.

References


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